

JAN

62198

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: My-Chan Tran Examiner #: 78933 Date: 3/12/02
 Art Unit: 1641 Phone Number 30 5-6999 Serial Number: 09/781,697
 Mail Box and Bldg/Room Location: CM1, 8A16 Results Format Preferred (circle): (PAPER) DISK E-MAIL
7E12

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Biosensor Compositions and Methods of Use
 Inventors (please provide full names): Hagan P. Bayley, ~~Step~~ Stefan G. Howorka,
and Liviu Movileanu

Earliest Priority Filing Date: 2/11/2000

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Jan,

Can you please perform the following searches:

- 1) Inventors search
- 2) Search attached claims

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Jan Delaval
 Reference Librarian
 Biotechnology & Chemical Library
 CM1 1E07 - 703-308-4498
 jan.delaval@uspto.gov

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Date Searcher Picked Up: <u>3/19/02</u>	Bibliographic <input checked="" type="checkbox"/>	Dr. Link _____
Date Completed: <u>3/19/02</u>	Litigation _____	Lexis/Nexis _____
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Online Time: <u>15</u>	Other _____	Other (specify) _____

=> fil wpix

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FILE LAST UPDATED: 13 MAR 2002 <20020313/UP>
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=> d all abeq tech tot

L71 ANSWER 1 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2002-026220 [03] WPIX
DNN N2002-020192 DNC C2002-007456
TI Transporting molecule, e.g. pharmaceuticals or glucose, through mammalian
barrier membrane e.g. human skin membrane, by ablating membrane with shear
device.
DC B07 P34 S05
IN COSTON, A F; KOLLIAS, N; SUN, Y
PA (JOHJ) JOHNSON & JOHNSON CONSUMER CO INC
CYC 93
PI WO 2001083027 A2 20011108 (200203)* EN 59p A61N001-30
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
ADT WO 2001083027 A2 WO 2001-US14054 20010501
PRAI US 2001-845956 20010430; US 2000-200839P 20000501
IC ICM A61N001-30
AB WO 200183027 A UPAB: 20020114
NOVELTY - Transporting a molecule through a mammalian barrier membrane
comprises ablating the membrane with a shear device having a sheet
containing at least one opening and shear blade. The sheet is contacted
with the membrane to force a membrane part through the opening and ablate
the membrane part exposed through the opening. A driving force is used to
move the molecule through the perforated membrane.
USE - Used for transporting a molecule e.g. pharmaceutical including
polysaccharides, **peptides**, **protein**, polynucleotides,
glucose or a vaccine (e.g., vaccine against **Staphylococcus**
aureus) through mammalian barrier membrane e.g., human skin, buccal,
vaginal, or rectal membranes. The molecule can be transported from within
the mammal out through the membrane.
ADVANTAGE - The method controls the transportation of molecules
across barrier membranes. The **pores** created by the shear
perforation method are not transient (e.g., in contrast to
electroporation), but permanent as these **pores** will remain open
until the new cells are re-grown over the opening. The method eliminates
the need for constant monitoring of the state of the transient microscopic
pores as in electroporation.
Dwg.0/9
FS CPI EPI GMPI
FA AB; DCN
MC CPI: B04-C01; B04-C02; B04-N04; B11-C09

EPI: S05-M

TECH

UPTX: 20020114

TECHNOLOGY FOCUS - BIOLOGY - Preferred Device: The device also comprises a **sensor**, which can be pressure, conductivity, impedance, pH, or temperature **sensor**. A feedback from the **sensor** modifies the driving unit. The **sensor** is an impedance **sensor** for detecting the impedance of the barrier membrane and relaying it to a microprocessor. The shear device comprises a driving unit to move the blade. The driving unit is powered manually or by an electric motor. The membrane portion is forced into the opening by a pressure force, preferably a mechanical pressure or suction. The driving force is iontophoresis, electro-osmosis, reverse iontophoresis, electroporation, phonophoresis, pressure gradients, or concentration gradients. The sheet blade moves parallel to the sheer sheet.

L71 ANSWER 2 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-589719 [66] WPIX

DNN N2001-439283 DNC C2001-174819

TI Modified, covalently-linked, sensing **pore**-subunit **polypeptides** useful for detecting and measuring analytes or physical characteristics within a sample, are capable of assembling into **pore** assemblies.

DC A96 B04 S03

IN BAYLEY, H P; HOWORKA, S G; MOVILEANU, L

PA (TEXA) UNIV TEXAS A & M SYSTEM

CYC 93

PI WO 2001059453 A2 20010816 (200166)* EN 90p G01N033-53

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001041474 A 20010820 (200175) G01N033-53

ADT WO 2001059453 A2 WO 2001-US4482 20010212; AU 2001041474 A AU 2001-41474 20010212

FDT AU 2001041474 A Based on WO 200159453

PRAI US 2000-182097P 20000211

IC ICM G01N033-53

AB WO 200159453 A UPAB: 20011113

NOVELTY - A modified **pore**-subunit **polypeptide** (I) comprising a **pore**-subunit **polypeptide** covalently linked to at least a sensing moiety, which assembles into an oligomeric **pore** assembly in the presence of several **pore**-subunit **polypeptides**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an oligomeric **pore** assembly (II) comprising several (I) sufficient to form a **pore**; and (2) a **biosensor** device comprising (II).

USE - The modified **pore**-subunit **polypeptides** are capable of assembling into **pores** or oligomeric **pore** assemblies which are useful for detecting the presence of an analyte, especially an oligonucleotide in a sample, by contacting the sample with (II) and detecting an electrical current through a first channel, where the modulation in current compared to a current measurement in a control sample lacking the analyte indicates the presence of the analyte in the sample. They are useful for detecting and quantitating the presence of an unknown analyte in a sample, by detecting an electric current through single or at least two channels to determine a sample current signature and comparing the signature to a standard current signature of a known analyte, where the concurrence of the sample and standard current signatures indicates identity of unknown analyte. (II) is also useful for detecting a change in the type or amount of biological or chemical constituent in the sample or physical environment of the sample. The method involves contacting the sample with (II) at a two time points,

determining two sample current signatures by detection of an electrical current through a first channel in continuous flow mode, comparing the sample current signatures, where a difference between the signatures indicates a change in the type or amount of biological or chemical constituent in the sample or physical environment of the sample (claimed). The **biosensor** devices are useful for detecting changes in ionic current flow, to detect, quantitate and/or discriminate between components driven through the **pore** by an applied potential and for detecting any analyte, component or physical parameter that contacts or impacts the measurable channel of the **pore** assembly.

Dwg.0/9

FS CPI EPI

FA AB; DCN

MC CPI: A12-V03C2; B04-B01B; B04-B03C; **B04-C01**; B04-C02; B04-C02X;
B04-C03C; B04-E01; B04-G01; B04-L01; B06-F03; B11-C08; B12-K04
EPI: S03-E14H4

TECH UPTX: 20011113

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Polypeptide**: (I) is

staphylococcal hemolysin polypeptide, porin,

complement **pore polypeptide**, hemolysin C

polypeptide or **streptolysin O polypeptide**,

preferably a mutant **staphylococcal alpha-hemolysin**

polypeptide comprising a first heterologous amino acid. The mutant

polypeptide comprises a cysteine residue in place of serine at

position 106 or **lysine** at position 8 of the wild-type

staphylococcal alpha-hemolysin polypeptide.

The sensing moiety is a functional group, such as a synthetic molecule, e.g. calixarene or crown ether, a naturally occurring molecule e.g. enzyme inhibitor, hapten, nucleotide, amino acid, lipid, toxin, saccharide, chelator or cyclodextrin or is a polymer e.g. polyethylene glycol (PEG)-biotin, analyte-binding polymer, oligonucleotide, oligosaccharide or

peptide. The sensing moiety binds to a metal, metal ion, toxin,

enzyme, nucleotide, oligonucleotide, amino acid, **peptide**,

saccharide, hapten, lipid or antibody or its antigen-binding fragment and

responds to a change in the type or amount of a biological or chemical

constituent in the environment or physical environment of (II), such as

pH, voltage, light or temperature. (I) is covalently linked to same or

different sensing moieties. (II) comprises several modified **pore**

-subunit **polypeptides**, preferably 7 **pore**-subunit

polypeptides.

L71 ANSWER 3 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2000-387818 [33] WPIX

DNC C2000-117822

TI Analytical system for rapid detection and identification of analytes based upon spore germination, comprises using a reaction mixture containing microbial spore which can sense analyte specific signals.

DC B04 D16

IN ROTMAN, M B

PA (ROTM-I) ROTMAN M B

CYC 23

PI WO 2000029610 A1 20000525 (200033)* EN 37p C12Q001-02

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA JP

AU 2000016273 A 20000605 (200042) C12Q001-02

US 6228574 B1 20010508 (200128) C12Q001-00

EP 1131462 A1 20010912 (200155) EN C12Q001-02

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT WO 2000029610 A1 WO 1999-US27214 19991116; AU 2000016273 A AU 2000-16273

19991116; US 6228574 B1 US 1998-193385 19981117; EP 1131462 A1 EP

1999-959015 19991116, WO 1999-US27214 19991116

FDT AU 2000016273 A Based on WO 200029610; EP 1131462 A1 Based on WO 200029610

PRAI US 1999-134781P 19990519; US 1998-193385 19981117

IC ICM C12Q001-00; C12Q001-02

ICS C12Q001-68; C12Q001-70

AB WO 200029610 A UPAB: 20000712

NOVELTY - A method for detecting the presence of a suspected analyte in a test sample, comprising combining a test sample containing the suspected analyte, with a reaction mixture comprising microbial spores that can sense an analyte-specific signal and respond to it by establishing an analyte-independent signal amplification system, and a germinogenic source, is new.

DETAILED DESCRIPTION - The mixture is incubated to allow enzymatic conversion of the germinogenic source to a germinant, and for spore germination. Spore germination is detected by a measurable parameter, where the suspected analyte is capable of generating a germinant by enzymatic action on the germinogenic source.

USE - The method is used to detect the presence and quantity of specific target analytes, (claimed) e.g. microbes such as bacteria (e.g. *Enterobacter aerogenes*, *Escherichia coli*, *Chlamydia trachomatis*, *Clostridium*, *Haemophilus influenza*, *Klebsiella pneumoniae*, *Neisseria gonorrhoeae*, *Salmonella*, and *Staphylococcus*), fungi (e.g. *Aspergillus fumigatus*, *Blastomyces dermatitidis*, *Candida albicans*, and *Trichomonas vaginalis*) and protozoa, viruses (e.g. cytomegalovirus, hepatitis virus, herpes virus, and human immunodeficiency virus), nucleic acid macromolecules (e.g. DNA or RNA), **proteins**, and naturally soluble macromolecules (e.g. chemokines, cytokines, growth factors, hormones). The analyte must be capable of generating a germinant by enzymatic action on a germinogenic source.

ADVANTAGE - The present invention reduces the time and cost of prior art analytical tools, resulting in faster diagnosis. The invention does not require growth of vegetative bacterial cells since it depends exclusively on spore germination, and does not require enzyme-labeled probes.

DESCRIPTION OF DRAWING(S) - The figure is a diagrammatical view of a **biosensor** used in the invention. The figure includes a top view and two cross-sectional views of portions of the **biosensor**.

Biosensor 10

Mesh 12

Membrane filter 14

0.2 μ m pores 15

Microwells 16

Suspension 18.

Dwg.1/1

FS CPI

FA AB; GI; DCN

MC CPI: B04-E02; B04-F06; B04-F09A; B04-F10; B04-F10A3; B04-F10A5; B04-F10A8; B04-F10B3; B04-F11; B04-H01; B04-H06; B04-L01; B11-C08E1; D05-A02; D05-H04; D05-H05; D05-H06; D05-H09

TECH UPTX: 20000712

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The microbial spores can be natural, or genetically modified to carry a chromosomal gene selected from a lux bioluminescence gene which only becomes bioluminescent upon germination, a lac gene which only produces a reporter enzyme upon germination, and a fluorescent protein coding gene which only produces the fluorescent protein upon germination. The spores are produced by bacteria or fungi. The germinant source is converted to the germinant by contact with at least one enzyme. Alternatively, a complex germinogenic source is used where an enzyme generates a reaction product which is converted into a germinant in the presence of one or more addition molecules. The suspected analyte is initially incapable of generating a germinant by enzymatic reaction on a germinogenic source, and becomes capable during the method, or by means of a germinogenic enzyme attached to the analyte. The analyte naturally produces an enzyme which results in the enzymatic conversion of the germinogenic source to germinant. Prior to combining, the spores are processed to be devoid of active germinant. Detection is by loss of spore biofringence, or by the appearance of enzymatic activity due to an enzyme which is synthesized de novo or activated in the germinating spores.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Analyte: The suspected analyte is a microbe, virus, an insoluble nucleic acid macromolecule, or naturally

soluble macromolecule which has been immobilized in or on discrete particles. The analyte us DNA specifically labeled using complementary oligonucleotides linked to a germinogenic enzyme by biotin-avidin bonds.

L71 ANSWER 4 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1999-153311 [13] WPIX
 DNN N1999-110551 DNC C1999-045198
 TI New mutant **staphylococcal alpha-haemolysin** - comprises
 a heterologous amino acid that binds to analyte, particularly metal ions.
 DC B04 D15 D16 E19 E37 J04 K04 S03
 IN **BAYLEY, H**; **BRAHA, O**; **GOUAUX, E**; **KASIANOWICZ, J**
 PA (UYMA-N) UNIV MASSACHUSETTS
 CYC 22
 PI WO 9905167 A1 19990204 (199913)* EN 50p C07K014-195
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: AU CA JP KR
 AU 9885862 A 19990216 (199926) C07K014-195
 ADT WO 9905167 A1 WO 1998-US15354 19980724; AU 9885862 A AU 1998-85862
 19980724
 FDT AU 9885862 A Based on WO 9905167
 PRAI US 1997-53737P 19970725
 IC ICM C07K014-195
 ICS C07K014-305; C07K014-31; G01N033-20; G01N033-48
 AB WO 9905167 A UPAB: 19990331
 New mutant **staphylococcal alpha -haemolysin (aHL)**
polypeptide (I): (i) includes a heterologous amino acid (HAA) that
 binds an analyte, and (ii) assembles into a heteroheptameric **pore**
 assembly in presence of many wild-type aHL **polypeptides**. Also
 new are: (1) aHL **polypeptide (Ia)** with at least two
 non-consecutive HAA in its stem domain, each of which binds: (i) a metal,
 or (ii) an organic compound; (2) heptameric **pore** assemblies
 (HPA) containing (I), and (3) digital **biosensors** comprising HPA.
 USE - The **biosensors** are particularly used to detect and
 quantify metal ions (specifically zinc, cobalt, nickel and cadmium), e.g.
 in water (for micronutrient analysis), sediment, air, industrial effluent.
 Organic compounds that can be detected are specifically explosives, but
 may also be macromolecules or entire bacteria or viruses.
 ADVANTAGE - **Pore-forming bacterial proteins** such
 as aHL are robust and provide an information-rich signal by single-channel
 recording. The binding site in (I) need not be strictly specific, since
 the kinetics, extent and voltage-dependence of the channel blockade
 provides a differential analysis, allowing several measurements to be made
 simultaneously. Compared with conventional analogue/steady state
biosensors, the new devices have a much wider dynamic range (over
 10000-fold, compared with about 20-fold, since the quality of the signal
 is independent of site occupancy and simultaneous occupation with
 different analytes can not occur). The digital mode allows operation in
 real chemical time and the **biosensors** are sensitive (in the
 nanomolar range), rapid, reversible and selective.
 Dwg.0/8
 FS CPI EPI
 FA AB; DCN
 MC CPI: **B04-C01**; **B04-F10**; **B04-F11**; **B04-N02**; **B05-A03A**; **B12-K04**;
D05-H04; **D05-H06**; **E10-B02D**; **E35-C**; **J04-C04**; **K04-F**
 EPI: **S03-E14C**; **S03-E14H**

L71 ANSWER 5 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1996-251085 [25] WPIX
 CR 1995-014066 [02]
 DNC C1996-079455
 TI Prepn. of synthetic ion channels - by coupling active ion channel peptide
 sub units to a polypeptide backbone.
 DC B04 J04
 IN MONTAL, M; TOMICH, J
 PA (SYNP-N) SYNPORIN TECHNOLOGIES INC
 CYC 1

PI US 5516890 A 19960514 (199625)* 31p A61K038-04
 ADT US 5516890 A CIP of US 1989-430814 19891102, Div ex US 1990-576222
 19900831, US 1994-312821 19940927
 FDT US 5516890 A Div ex US 5368712
 PRAI US 1990-576222 19900831; US 1989-430814 19891102; US 1994-312821
 19940927
 IC ICM A61K038-04
 ICS C07K005-00; C07K007-00
 AB US 5516890 A UPAB: 19960625
 (A) A sequential method for prepg. a **polypeptide** backbone and active ion channel subunits comprises (a) prepg. a **polypeptide** backbone portion having 1-10 amino acids, (b) reacting a terminal NH₂ gp. of the backbone portion with a first t-Boc and Fmoc subst. amino acid, (c) deprotecting the t-Boc NH₂ residue, (d) introducing an active **peptide** subunit onto the t-Boc deprotected NH₂ residue, (e) deprotecting the Fmoc NH₂ residue, (f) introducing a backbone **protein** sequence onto the deprotected Fmoc NH₂ residue, (g) reacting a second t-Boc and Fmoc subst. amino acid and backbone terminal NH₂ residue, (h) deprotecting the t-Boc NH₂ residue of the second Fmoc and t-Boc subst. amino acid, and (i) introducing an active **peptide** subunit onto the deprotected t-Boc NH₂ residue. Also claimed are (B) a **peptide** comprising D-P-W-N-V-F-D-F-L-I-V-I-S-S-I-I-D-V-I-L-S-G (I) or A-R-T-V-F-G-V-T-T-V-L-T-M-T-T-L-S-T-S-A-R (II); and (C) a **peptide** template comprising B'[(X)nB']_m (III) or (X)n[B'(X)n]_m (IV), in which B' = a basic amino acid having a terminal amino gp. which is bound to a protective gp., X = any arbitrary amino acid, and m and n = 1-10.

USE - The synthetic channel ion **proteins** can be used for testing properties of pharmacological cpds. or for the presence of particular cpds. or characteristics. They are used partic. for the prodn. of **biosensors**.

ADVANTAGE - The synthetic **polypeptides** have a sequence ordered to form an active interior **pore** surface with surrounding molecular structures such that they have response characteristics mimetic to a chosen native channel even though the synthetic channel does not comprise the whole native channel but uses only selected subunits.
 Dwg.0/15

FS CPI
 FA AB; DCN
 MC CPI: B04-C01; B04-N04A; B11-C08; B12-K04; J04-B01B; J04-C04

L71 ANSWER 6 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1995-014066 [02] WPIX

CR 1996-251085 [25]

DNN N1995-010995 DNC C1995-006313

TI Synthetic ion channel assembly contg. synthetic protein - comprising template and tethered peptide chains incorporated into lipid bi layer, accurately mimicking native channels, and **bio sensor** (s) based on it.

DC B04 J04 S03

IN MONTAL, M; TOMICH, J

PA (SYNP-N) SYNPORIN TECHNOLOGIES INC

CYC 1

PI US 5368712 A 19941129 (199502)* G01N027-327

ADT US 5368712 A CIP of US 1989-430814 19891102, US 1990-576222 19900831

PRAI US 1990-576222 19900831; US 1989-430814 19891102

IC ICM G01N027-327

AB US 5368712 A UPAB: 19960705

A novel synthetic assembly for in vitro active ion transport, mimicking a native ion channel, comprises: (1) electrically insulating membrane; and (2) many synthetic **protein** units (I), transmembranelly dispersed in the membrane, each (I) contg. a template **peptide** (TP) and 4-10 **polypeptide** subunits (Ia) tethered to it, mimicking an active part of a native ion channel **protein** and positioned to extend from TP through the membrane. These structures define (a) a gated ion channel **pore** and (b) a detector region associated with the

pore.

USE - The **biosensors** are used for in vitro detection, and determin., of physiologically active substances such as antiseptics, antibiotics and neurotransmitters, also toxins, insecticides, food additives, etc..

ADVANTAGE - These synthetic channels are less expensive than native structures but still provide a response that accurately represents physiological response. (I) are self-assembling, stable and robust, and can be prepd. in any desired quantity.

Dwg.7/15

FS CPI EPI

FA AB; DCN

MC CPI: **B04-C01**; B04-N02; B05-A01A; B05-A01B; B10-B02; B11-C08B;

B11-C08E; B12-K04A; J04-C04

EPI: S03-E03C; S03-E14H

=> fil hcaplus

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FILE COVERS 1907 - 19 Mar 2002 VOL 136 ISS 12

FILE LAST UPDATED: 18 Mar 2002 (20020318/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> d all tot

L82 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:871429 HCAPLUS

TI Prolonged residence time of a noncovalent molecular adapter, .beta.-cyclodextrin, within the lumen of mutant .alpha.-**hemolysin pores**

AU Gu, Li-Qun; Cheley, Stephen; **Bayley, Hagan**

CS Department of Medical Biochemistry and Genetics, The Texas A and M University System Health Science Center, College Station, TX, 77843, USA

SO J. Gen. Physiol. (2001), 118(5), 481-493

CODEN: JGPLAD; ISSN: 0022-1295

PB Rockefeller University Press

DT Journal

LA English

CC 7 (Enzymes)

AB Noncovalent mol. adapters, such as cyclodextrins, act as binding sites for channel blockers when lodged in the lumen of the .alpha.-hemolysin (.alpha.HL) pore, thereby offering a basis for the detection of a variety of org. mols. with .alpha.HL as a sensor element. .beta.-Cyclodextrin (.beta.CD) resides in the wild-type .alpha.HL pore for several hundred microseconds. The residence time can be extended to several milliseconds by the manipulation of pH and transmembrane potential. Here, we describe mutant homoheptameric .alpha.HL pores that are capable of accommodating .beta.CD for tens of seconds. The mutants were obtained by site-directed mutagenesis at position 113, which is a residue that lies near a constriction in the lumen of the transmembrane .beta. barrel, and fall into two classes. Members of the tight-binding class, M113D, M113N, M113V, M113H, M113F and M113Y, bind .beta.CD .apprx.104-fold more avidly than the remaining .alpha.HL pores, including WT-.alpha.HL. The lower Kd values of these mutants are dominated by reduced values of koff. The major effect of the mutations is most likely a remodeling of the binding site for .beta.CD in the vicinity of position 113. In addn., there is a smaller voltage-sensitive component of the binding, which is also affected by the residue at 113 and may result from transport of the neutral .beta.CD mol. by electroosmotic flow. The mutant pores for which the dwell time of .beta.CD is prolonged can serve as improved components for stochastic sensors.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bath, B; Anal Chem 1998, V70, P1047 HCAPLUS
- (2) Bath, B; Anal Chem 2000, V72, P443
- (3) Bayley, H; Adv Mater 2000, V12, P139 HCAPLUS
- (4) Bayley, H; Bioorg Chem 1995, V23, P340 HCAPLUS
- (5) Bayley, H; Curr Opin Biotechnol 1999, V10, P94 HCAPLUS
- (6) Bayley, H; Nature 2001, V413, P226 HCAPLUS
- (7) Bayley, H; Sci Am 1997, V277, P62 HCAPLUS
- (8) Bezrukov, S; FEBS Lett 2000, V476, P224 HCAPLUS
- (9) Bhakdi, S; Proc Natl Acad Sci USA 1981, V78, P5475 HCAPLUS
- (10) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (11) Braha, O; Nat Biotechnol 2000, V17, P1005
- (12) Cheley, S; Protein Eng 1997, V10, P1433 HCAPLUS
- (13) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
- (14) Creighton, T; Proteins: Structures and Molecular Properties 1993, P507
- (15) D'Souza, V; Chem Rev 1998, V98, P1741 HCAPLUS
- (16) Eroglu, A; Nat Biotechnol 2000, V18, P163 HCAPLUS
- (17) Fussle, R; J Cell Biol 1981, V91, P83 MEDLINE
- (18) Gu, L; Biophys J 2000, V79, P1967 HCAPLUS
- (19) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (20) Gu, L; Proc Natl Acad Sci USA 2000, V97, P3959 HCAPLUS
- (21) Gu, L; Science 2001, V291, P636 HCAPLUS
- (22) Howorka, S; Nat Biotechnol 2001, V19, P636 HCAPLUS
- (23) Howorka, S; Proc Natl Acad Sci USA, In press 2001
- (24) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (25) Katchalsky, A; Nonequilibrium Thermodynamics in Biophysics 1965
- (26) Krasilnikov, O; J Membr Biol 1997, V156, P157 HCAPLUS
- (27) Montal, M; Proc Natl Acad Sci USA 1972, V69, P3561 HCAPLUS
- (28) Movileanu, I; Nat Biotechnol 2000, V18, P1091
- (29) Otto-Bruc, A; Proc Natl Acad Sci USA 1998, V95, P15014 HCAPLUS
- (30) Panchal, R; Nat Biotechnol 1996, V14, P852 HCAPLUS
- (31) Russo, M; Nat Biotechnol 1997, V15, P278 HCAPLUS
- (32) Sanchez-Quesada, J; J Am Chem Soc 2000, V122, P11758
- (33) Song, L; Science 1996, V274, P1859 HCAPLUS
- (34) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS
- (35) Walker, B; Proc Eng 1994, V7, P91 HCAPLUS

L82 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:858309 HCAPLUS

DN 136:130977

TI Kinetics of duplex formation for individual DNA strands within a single **protein** nanopore

AU **Howorka, Stefan; Movileanu, Liviu; Braha, Orit; Bayley, Hagan**

CS Department of Medical Biochemistry and Genetics, The Texas A and M University System Health Science Center, College Station, TX, 77843-1114, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(23), 12996-13001
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 9-2 (Biochemical Methods)

AB A single **oligonucleotide** was covalently attached to a genetically engineered subunit of the heptameric **protein pore, .alpha.-hemolysin**, to allow DNA duplex formation inside the **pore** lumen. Single-channel current recording was used to study the properties of the modified **pore**. On addn. of an **oligonucleotide** 8 bases in length and with a sequence complementary to the tethered DNA strand, current blockades with durations of hundreds of milliseconds occurred, representing hybridization events of individual **oligonucleotides** to the tethered DNA strand. Kinetic consts. for DNA duplex formation at the single mol. level were derived and found to be consistent with established literature values for macroscopic duplex formation. The resultant equil. const. for duplex formation in the nanopore was found to be close to the exptl. derived const. for duplex formation in soln. A good agreement between the equil. consts. for duplex formation in the nanopore and in soln. was also found for two other **oligonucleotide** pairs. In addn., the nanopore recordings revealed details of the kinetics difficult to obtain by conventional methods, like surface plasmon resonance, which measure ensemble properties. By investigating the temp. dependence of DNA duplex formation at the single mol. level, the std. enthalpy and entropy of the interaction could be obtained.

ST DNA duplex formation kinetics **hemolysin alpha** nanopore

IT DNA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(double-stranded; kinetics of duplex formation for individual DNA strands within a single **protein** nanopore)

IT Free energy
Molecular association
(kinetics of duplex formation for individual DNA strands within a single **protein** nanopore)

IT **Biosensors**
(surface plasmon-based; kinetics of duplex formation for individual DNA strands within a single **protein** nanopore)

IT **Hemolysins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.-; kinetics of duplex formation for individual DNA strands within a single **protein** nanopore)

IT 354584-62-6 354584-63-7 392247-81-3 392247-83-5 392247-84-6
392247-85-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(kinetics of duplex formation for individual DNA strands within a single **protein** nanopore)

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Akeson, M; Biophys J 1999, V77, P3227 HCAPLUS
- (2) Ambrose, W; Chem Rev 1999, V99, P2929 HCAPLUS
- (3) Ausubel, F; Current Protocols in Molecular Biology 1987, V1, P2.7.1
- (4) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (5) Braunlin, W; Biochemistry 1991, V30, P754 HCAPLUS
- (6) Breslau, K; Biophys Chem 1977, V7, P211 HCAPLUS

- (7) Cantor, C; Biophysical Chemistry Part III, The Behavior of Biological Macromolecules 1980
 - (8) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
 - (9) Clausen-Schaumann, H; Curr Opin Chem Biol 2000, V4, P524 HCAPLUS
 - (10) Colquhoun, D; Single-Channel Recording 1995, P483
 - (11) Corey, D; Bioconjug Chem 1995, V6, P93 HCAPLUS
 - (12) Deamer, D; Trends Biotechnol 2000, V18, P147 HCAPLUS
 - (13) Dumas, F; Proc Natl Acad Sci USA 2001, V98, P485 HCAPLUS
 - (14) Eggeling, C; Proc Natl Acad Sci USA 1998, V95, P1556 HCAPLUS
 - (15) Eigen, M; Proc Natl Acad Sci USA 1994, V91, P5740 HCAPLUS
 - (16) Gilles, P; Nat Biotechnol 1999, V17, P365 HCAPLUS
 - (17) Henrickson, S; Phys Rev Lett 2000, V85, P3057 HCAPLUS
 - (18) Hille, B; Ionic Channels of Excitable Membranes 1992
 - (19) Howorka, S; J Am Chem Soc 2000, V122, P2411 HCAPLUS
 - (20) Howorka, S; J Biol Chem 2000, V275, P37876
 - (21) Howorka, S; Nat Biotechnol 2001, V19, P636 HCAPLUS
 - (22) Jensen, K; Biochemistry 1997, V36, P5072 HCAPLUS
 - (23) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
 - (24) Kinjo, M; Nucleic Acids Res 1995, V23, P1795 HCAPLUS
 - (25) Li, A; Biophys J 1998, V74, P964 HCAPLUS
 - (26) Liphardt, J; Science 2001, V292, P733 HCAPLUS
 - (27) Martin, F; J Mol Biol 1971, V57, P201 HCAPLUS
 - (28) Meller, A; Phys Rev Lett 2001, V86, P3435 HCAPLUS
 - (29) Meller, A; Proc Natl Acad Sci USA 2000, V97, P1079 HCAPLUS
 - (30) Moczydlowski, E; Ion Channel Reconstitution 1986, P75
 - (31) Movileanu, L; Nat Biotechnol 2000, V18, P1091 HCAPLUS
 - (32) Nelson, J; Biochemistry 1982, V21, P5289 HCAPLUS
 - (33) Nie, S; Annu Rev Biophys Biomol Struct 1997, V26, P567 HCAPLUS
 - (34) Parkhurst, K; Biochemistry 1995, V34, P285 HCAPLUS
 - (35) Porschke, D; Biophys Chem 1974, V2, P97 MEDLINE
 - (36) Porschke, D; Biopolymers 1971, V10, P1989
 - (37) Porschke, D; J Mol Biol 1971, V62, P361 MEDLINE
 - (38) Rief, M; Nat Struct Biol 1999, V6, P346 HCAPLUS
 - (39) Riesner, D; Physico-Chemical Properties of Nucleic Acids 1973, V2, P237 HCAPLUS
 - (40) Schuck, P; Annu Rev Biophys Biomol Struct 1997, V26, P541 HCAPLUS
 - (41) Smith, S; Science 1996, V271, P795 HCAPLUS
 - (42) Song, L; Science 1996, V274, P1859 HCAPLUS
 - (43) Sosnowski, R; Proc Natl Acad Sci USA 1997, V94, P1119 HCAPLUS
 - (44) Strunz, T; Proc Natl Acad Sci USA 1999, V96, P11277 HCAPLUS
 - (45) Szabo, I; FASEB J 1998, V12, P495 HCAPLUS
 - (46) Vercoutere, W; Nat Biotechnol 2001, V19, P248 HCAPLUS
 - (47) Woodhull, A; J Gen Physiol 1973, V61, P687 HCAPLUS
 - (48) Wright Lucas, S; Anal Biochem 2000, V282, P70 HCAPLUS
- L82 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2002 ACS
- AN 2001:708018 HCAPLUS
- DN 135:238715
- TI Stochastic **sensors** inspired by biology
- AU **Bayley, Hagan**; Cremer, Paul S.
- CS Department of Medical Biochemistry and Genetics, The Texas A and M University System Health Science Center, College Station, TX, 72843-1114, USA
- SO Nature (London, United Kingdom) (2001), 413(6852), 226-230
CODEN: NATUAS; ISSN: 0028-0836
- PB Nature Publishing Group
- DT Journal; General Review
- LA English
- CC 9-0 (Biochemical Methods)
Section cross-reference(s): 1, 4
- AB A review with .apprx.54 refs. Sensory systems use a variety of membrane-bound receptors, including responsive ion channels, to discriminate between a multitude of stimuli. Here we describe how engineered membrane **pores** can be used to make rapid and sensitive **biosensors** with potential applications that range from the detection of biol. warfare agents to pharmaceutical screening.

Notably, use of the engineered **pores** in stochastic sensing, a single-mol. detection technol., reveals the identity of an analyte as well as its concn.

ST stochastic **sensor** review

IT **Biosensors**

(stochastic **sensors** inspired by biol.)

IT Ion channel

Sensory receptors

RL: ARU (Analytical role, unclassified); ANST (Analytical study)

(stochastic **sensors** inspired by biol.)

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Akeson, M; Biophys J 1999, V77, P3227 HCAPLUS
- (2) Ball, P; Nature 2001, V409, P413 HCAPLUS
- (3) Bayley, H; Adv Mater 2000, V12, P139 HCAPLUS
- (4) Bayley, H; Chem Rev 2000, V100, P2575 HCAPLUS
- (5) Bezrukov, S; J Membr Biol 2000, V174, P1 HCAPLUS
- (6) Boxer, S; Curr Opin Chem Biol 2000, V4, P704 HCAPLUS
- (7) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (8) Braha, O; Nature Biotechnol 2000, V17, P1005
- (9) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
- (10) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (11) Cremer, P; J Am Chem Soc 1999, V121, P8130 HCAPLUS
- (12) Deamer, D; Trends Biotechnol 2000, V18, P147 HCAPLUS
- (13) Dickinson, T; Nature 1996, V382, P687
- (14) Figeys, D; Analyt Chem 2000, V72, P330A HCAPLUS
- (15) Fisher, T; Neuron 2000, V27, P435 HCAPLUS
- (16) Glazier, S; Langmuir 2000, V16, P10428 HCAPLUS
- (17) Gu, I; Nature 1999, V398, P686
- (18) Gu, L; Science 2001, V291, P636 HCAPLUS
- (19) Henrickson, S; Phys Rev Lett 2000, V85, P3057 HCAPLUS
- (20) Hirn, R; Faraday Disc 1998, V111, P17 HCAPLUS
- (21) Hladky, S; Nature 1970, V225, P451 HCAPLUS
- (22) Horman, S; Chem Eng News 2000, P48
- (23) Howorka, S; Nature Biotechnol 2001, V19, P636 HCAPLUS
- (24) Hulteen, J; J Am Chem Soc 1998, V120, P6603 HCAPLUS
- (25) Hume, R; Nature 1983, V305, P632 HCAPLUS
- (26) Ide, T; Biochem Biophys Res Commun 1999, V265, P595 HCAPLUS
- (27) Iirage, K; Science 1997, V278, P655
- (28) Kasianowicz, J; Proc Natl Acad Sci 1996, V93, P13770 HCAPLUS
- (29) Kodadek, T; Chem Biol 2001, V8, P105 HCAPLUS
- (30) Kramer, R; Neuron 1990, V4, P335 HCAPLUS
- (31) Li, J; Nature 2001, V412, P166 HCAPLUS
- (32) Lucas, S; Analyt Biochem 2000, V282, P70
- (33) McGeoch, J; Med Biol Eng Comput 2000, V38, P113 MEDLINE
- (34) Mehta, A; Science 1999, V283, P1689 HCAPLUS
- (35) Meller, A; Proc Natl Acad Sci 2000, V97, P1079 HCAPLUS
- (36) Movileanu, L; Nature Biotechnol 2000, V18, P1091 HCAPLUS
- (37) Sackmann, E; Science 1996, V271, P43 HCAPLUS
- (38) Sackmann, E; Trends Biotechnol 2000, V18, P58 HCAPLUS
- (39) Sanchez-Quesada, J; J Am Chem Soc 2000, V122, P11758
- (40) Schmidt, C; Angew Chem Int Edn 2000, V39, P3137 HCAPLUS
- (41) Schuster, B; Biochim Biophys Acta 1998, V1370, P280 HCAPLUS
- (42) Schustes, B; Langmuir 2001, V17, P499
- (43) Stora, T; Angew Chem Int Edn 1999, V38, P389 HCAPLUS
- (44) Straub, B; Nature Biotechnol 2001, V19, P121 HCAPLUS
- (45) Sun, L; J Am Chem Soc 2000, V122, P12340 HCAPLUS
- (46) Tonucci, R; Science 1992, V258, P783 HCAPLUS
- (47) Trivedi, B; Neuron 1998, V21, P895 HCAPLUS
- (48) Vercoutete, W; Nature Biotechnol 2001, V19, P248
- (49) Weiss, S; Science 1999, V283, P1676 HCAPLUS
- (50) Wiegand, G; Rev Sci Instrum 2000, V71, P2309 HCAPLUS
- (51) Xie, X; J Biol Chem 1999, V274, P15967 HCAPLUS
- (52) Yang, T; Analyt Chem 2000, V72, P2587 HCAPLUS
- (53) Yang, T; Analyt Chem 2001, V73, P165 HCAPLUS
- (54) Young, S; Nature 1983, V305, P634 HCAPLUS

L82 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2002 ACS
 AN 2001:598294 HCAPLUS
 DN 135:177670

TI **Biosensors with pore peptide compositions**
 and methods of use

IN **Bayley, Hagan P.; Howorka, Stefan G.; Movileanu, Liviu**

PA The Texas A + M University System, USA

SO PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-53

CC 9-1 (Biochemical Methods)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001059453	A2	20010816	WO 2001-US4482	20010212
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2000-182097P P 20000211

AB The present invention relates generally to detection of one or more analytes in a sample and/or the magnitude of or changes in phys. properties of a sample. More particularly, it concerns **pore**-subunit **polypeptides** covalently linked to one or more sensing moieties, and the use of these modified **polypeptides** to detect and/or measure analytes or certain phys. characteristics within a given sample. Provided are **pore**-subunit **polypeptides** covalently linked to one or more sensing moieties, and uses of these modified **polypeptides** as described.

ST **biosensor pore modified polypeptide**
staphylococcal hemolysin polymer

IT **Biosensors**

Chelating agents

Functional groups

Ions

Light

Molecular association

Molecular recognition

Temperature

pH

(**Biosensors with pore peptide** compns. and methods of use)

IT DNA

RL: ANT (Analyte); ANST (Analytical study)

(**Biosensors with pore peptide** compns. and methods of use)

IT Amino acids, analysis

Haptens

Lipids, analysis

Nucleotides, analysis

Oligonucleotides

Oligosaccharides, analysis

Peptides, analysis

Toxins

RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)

(**Biosensors with pore peptide** compns. and

- methods of use)
- IT Antibodies
Crown ethers
Enzymes, uses
Hemolysins O
Metals, uses
Polymers, uses
Polyoxyalkylenes, uses
Polysaccharides, uses
Porins
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**Biosensors** with **pore peptide** compns. and
methods of use)
- IT **Hemolysins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(C; **Biosensors** with **pore peptide** compns.
and methods of use)
- IT Metacyclophanes
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(calixarenes; **Biosensors** with **pore peptide**
compns. and methods of use)
- IT Enzymes, uses
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(inhibitors; **Biosensors** with **pore peptide**
compns. and methods of use)
- IT **Proteins**, general, uses
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**polypeptide**; **Biosensors** with **pore**
peptide compns. and methods of use)
- IT Complement
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**pore**; **Biosensors** with **pore**
peptide compns. and methods of use)
- IT **Hemolysins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**staphylococcal**; **Biosensors** with **pore**
peptide compns. and methods of use)
- IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(transmembrane, **pore**; **Biosensors** with **pore**
peptide compns. and methods of use)
- IT **Hemolysins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**.alpha.-**, **staphylococcal**, mutant, with cysteine at
position 106; **Biosensors** with **pore peptide**
compns. and methods of use)
- IT **Hemolysins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**.alpha.-**, **staphylococcal**, mutant, with cysteine at
position 8; **Biosensors** with **pore peptide**
compns. and methods of use)
- IT **Hemolysins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST
(Analytical study); USES (Uses)
(**.alpha.-**, **staphylococcal**; **Biosensors**
with **pore peptide** compns. and methods of use)

IT 12619-70-4, cyclodextrin 25322-68-3, Polyethylene glycol
 RL: ARG (Analytical reagent use); DEV (Device component use); ANST
 (Analytical study); USES (Uses)
 (**Biosensors** with **pore peptide** compns. and
 methods of use)

IT 354648-02-5 354648-03-6 354648-04-7 354807-77-5, 2: PN: WO0159453
 SEQID: 7 unclaimed DNA 354807-78-6, 3: PN: WO0159453 SEQID: 8 unclaimed
 DNA 354807-80-0, 4: PN: WO0159453 SEQID: 9 unclaimed DNA 354807-82-2,
 6: PN: WO0159453 SEQID: 11 unclaimed DNA 354807-83-3, 7: PN: WO0159453
 SEQID: 12 unclaimed DNA 354807-84-4, 8: PN: WO0159453 SEQID: 13
 unclaimed DNA 354807-87-7, 9: PN: WO0159453 SEQID: 14 unclaimed DNA
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; **biosensors** with **pore
 peptide** compns. and methods of use)

IT 354584-61-5 354584-62-6 354584-63-7 354584-64-8
 RL: PRP (Properties)
 (unclaimed sequence; **biosensors** with **pore
 peptide** compns. and methods of use)

L82 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2002 ACS
 AN 2001:495050 HCAPLUS
 DN 136:145702
 TI Sequence-specific detection of individual DNA strands using engineered
 nanopores

AU **Howorka, Stefan**; Cheley, Stephen; **Bayley, Hagan**
 CS Department of Medical Biochemistry and Genetics, The Texas A&M University
 System Health Science Center, College Station, TX, 77843-1114, USA
 SO Nature Biotechnology (2001), 19(7), 636-639
 CODEN: NABIF9; ISSN: 1087-0156
 PB Nature America Inc.
 DT Journal
 LA English
 CC 3-1 (Biochemical Genetics)

AB We describe **biosensor** elements that are capable of identifying
 individual DNA strands with single-base resolu. Each **biosensor**
 element consists of an individual DNA **oligonucleotide** covalently
 attached within the lumen of the c-hemolysin (acHL) **pore**
 to form a "DNA-nanopore". The binding of single-stranded DNA (ssDNA)
 mols. to the tethered DNA strand causes changes in the ionic current
 flowing through a nanopore. On the basis of DNA duplex lifetimes, the
 DNA-nanopores are able to discriminate between individual DNA strands up
 to 30 nucleotides in length differing by a single base substitution. This
 was exemplified by the detection of a drug resistance-conferring mutation
 in the reverse transcriptase gene of HIV. In addn., the approach was used
 to sequence a complete codon in an individual DNA strand tethered to a
 nanopore.

ST **biosensor alpha hemolysin nanopore**
oligonucleotide conjugate sequencing mutation detection

IT DNA sequence analysis
 Nucleic acid hybridization
 (sequence-specific detection of individual DNA strands using engineered
 nanopores)

IT DNA
 RL: ANT (Analyte); ANST (Analytical study)
 (sequence-specific detection of individual DNA strands using engineered
 nanopores)

IT **Hemolysins**
 RL: ARG (Analytical reagent use); DEV (Device component use); ANST
 (Analytical study); USES (Uses)
 (.**alpha.-**, nanopores, **oligonucleotide** conjugates;
 sequence-specific detection of individual DNA strands using engineered
 nanopores)

IT **Biosensors**
 (.**alpha.-hemolysin nanopore-oligonucleotide**
 conjugate-contg.; sequence-specific detection of individual DNA strands
 using engineered nanopores)

IT 9068-38-6, Reverse transcriptase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV, drug resistance-conferring mutation in gene for;
sequence-specific detection of individual DNA strands using engineered
nanopores)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Aboul-ela, F; Nucleic Acids Res 1985, V13, P4811 HCAPLUS
- (2) Akesson, M; Biophys J 1999, V77, P3227 HCAPLUS
- (3) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (4) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
- (5) Corey, D; Bioconjug Chem 1995, V6, P93 HCAPLUS
- (6) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (7) Eigen, M; Proc Natl Acad Sci USA 1994, V91, P5740 HCAPLUS
- (8) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (9) Gu, L; Science 2001, V291, P636 HCAPLUS
- (10) Henrickson, S; Phys Rev Lett 2000, V85, P3057 HCAPLUS
- (11) Howorka, S; J Am Chem Soc 2000, V122, P2411 HCAPLUS
- (12) Hulteen, J; J Amer Chem Soc 1998, V120, P6603 HCAPLUS
- (13) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (14) Meller, A; Proc Natl Acad Sci USA 2000, V97, P1079 HCAPLUS
- (15) Movileanu, L; Nat Biotechnol 2000, V18, P1091 HCAPLUS
- (16) Quake, S; Science 2000, V290, P1536 HCAPLUS
- (17) Richman, D; J Virol 1994, V68, P1660 HCAPLUS
- (18) Rief, M; Nat Struct Biol 1999, V6, P346 HCAPLUS
- (19) Schmidt, C; Angew Chem Int Edn Engl 2000, V39, P3137 HCAPLUS
- (20) Smith, S; Science 1996, V271, P795 HCAPLUS
- (21) Song, L; Science 1996, V274, P1859 HCAPLUS
- (22) Stora, T; Angew Chem Int Edn Engl 1999, V38, P389 HCAPLUS
- (23) Strunz, T; Proc Natl Acad Sci USA 1999, V96, P11277 HCAPLUS
- (24) Vercoutere, W; Nat Biotechnol 2001, V19, P248 HCAPLUS

L82 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:209001 HCAPLUS

DN 135:368679

TI Microfinishing of channel **pore** and real time sensing

AU Futaki, Shiro

CS Institute for Chemical Research, Kyoto University, Japan

SO Kagaku (Kyoto, Japan) (2001), 56(3), 58-59

CODEN: KAKYAU; ISSN: 0451-1964

PB Kagaku Dojin

DT Journal; General Review

LA Japanese

CC 9-0 (Biochemical Methods)

AB A review with refs. on the application of the patch clamp method for real time quant. of polymeric substances such as **.alpha.-hemolysin protein** which can not pass through the channel **pore** by measuring the channel current through interaction with the polyethylene glycol (PEG) chain in the channel **pore**. A diagram for quant. of **.alpha.-hemolysin** using interaction between biotinylated PEG with streptavidin was given.

ST review channel current patch clamp method

IT Electric current

(channel; microfinishing of channel **pore** and real time sensing)

IT **Biosensors**

(microfinishing of channel **pore** and real time sensing).

IT Biopolymers

Ion channel

RL: ANT (Analyte); ANST (Analytical study)

(microfinishing of channel **pore** and real time sensing)

IT Polyoxyalkylenes, uses

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(microfinishing of channel **pore** and real time sensing)

IT **Hemolysins**

RL: ANT (Analyte); ANST (Analytical study)

(.alpha.-; microfinishing of channel **pore** and real time sensing)

IT 25322-68-3, Polyethylene glycol
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (microfinishing of channel **pore** and real time sensing)

L82 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2002 ACS
 AN 2001:73166 HCAPLUS
 DN 134:277064
 TI Capture of a single molecule in a nanocavity
 AU Gu, Li-Qun; Cheley, Stephen; **Bayley, Hagan**
 CS Department of Medical Biochemistry and Genetics, Texas A&M University
 System Health Science Center, College Station, TX, 77843, USA
 SO Science (Washington, DC, United States) (2001), 291(5504), 636-640
 CODEN: SCIEAS; ISSN: 0036-8075
 PB American Association for the Advancement of Science
 DT Journal
 LA English
 CC 6-3 (General Biochemistry)
 AB We describe a heptameric **protein pore** that has been engineered to accommodate two different cyclodextrin adapters simultaneously within the lumen of a transmembrane .beta. barrel. The vol. between the adapters is a cavity of .apprx.4400 cubic angstroms. Anal. of single-channel recordings reveals that individual charged org. mols. can be pulled into the cavity by an elec. potential. Once trapped, an org. mol. shuttles back and forth between the adapters for hundreds of milliseconds. Such self-assembling nanostructures are of interest for the fabrication of multianalyte **sensors** and could provide a means to control chem. reactions.

ST **hemolysin pore** self assembling nanostructure mol capture

IT Nanostructures
 (capture of a single mol. in a nanocavity)

IT Self-assembly
 (capture of a single mol. in self-assembling nanostructure)

IT Electric potential
 (elec. potential pulls charged org. mols. into nanocavity in engineered **protein pore**)

IT Free energy of activation
 (free energies of activation for interaction of 1,3-adamantane dicarboxylic acid with cyclodextrins lodged within engineered **protein pore**)

IT Dissociation constant
 (kinetics of cyclodextrin adapters assocn. with .alpha.-**hemolysin**)

IT **Hemolysins**
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (.alpha.-; capture of a single mol. in nanocavity formed in .alpha.-**hemolysin** M113N/N139Q)

IT 70-47-3, L-Asparagine, properties
 RL: PRP (Properties)
 (hepta-6-sulfato-.beta.-cyclodextrin assocn. with Asn139 in .alpha.-**hemolysin**)

IT 5511-18-2, 1-Adamantane carboxamide 39269-10-8, 1,3-Adamantane dicarboxylic acid
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (org. mol. shuttles back and forth between cyclodextrin adapters trapped in engineered **protein pore**)

IT 7585-39-9, .beta.-Cyclodextrin 184840-97-9
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (**protein pore** engineered to accommodate two different cyclodextrin adapters)

IT 63-68-3, L-Methionine, properties

RL: PRP (Properties)

(.beta.-cyclodextrin assoc. with Met113 in .alpha.-hemolysin)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Anon; Science, (www.sciencemag.org/cgi/content/full/291/5504/636/DC1)
- (2) Bayley, H; Adv Mater 2000, V12, P139 HCAPLUS
- (3) Braha, O; Nature Biotechnol 2000, V17, P1005
- (4) Gu, L; Biophys J 2000, V79, P1967 HCAPLUS
- (5) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (6) Gu, L; Proc Natl Acad Sci U S A 2000, V97, P3959 HCAPLUS
- (7) Hille, B; Ionic Channels of Excitable Membranes, ed 2 1991
- (8) Howorka, S; J Am Chem Soc 2000, V122, P2411 HCAPLUS
- (9) Moczydlowski, E; Ion Channel Reconstitution 1986, P75
- (10) Movileanu, L; Nature Biotechnol 2000, V18, P1091 HCAPLUS
- (11) Noji, H; Nature 1997, V386, P299 HCAPLUS
- (12) Olenyuk, B; Nature 1999, V398, P796 HCAPLUS
- (13) Rebek, J; Chem Commun 2000, V2000, P637
- (14) Rudkevich, D; Eur J Org Chem 1999, P1991 HCAPLUS
- (15) Sanchez-Quesada, J; J Am Chem Soc 2000, V122, P11757 HCAPLUS
- (16) Song, L; Science 1996, V274, P1859 HCAPLUS
- (17) Soong, R; Science 2000, V290, P1555 HCAPLUS
- (18) Takeda, N; Nature 1999, V398, P794 HCAPLUS
- (19) Woodhull, A; J Gen Physiol 1973, V61, P687 HCAPLUS

L82 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:737319 HCAPLUS

DN 134:53412

TI Detecting **protein** analytes that modulate transmembrane movement of a polymer chain within a single **protein pore**

AU **Movileanu, Liviu; Howorka, Stefan; Braha, Orit; Bayley, Hagan**

CS Department of Medical Biochemistry and Genetics, The Texas A&M University System Health Science Center, College Station, TX, 77843-1114, USA

SO Nature Biotechnology (2000), 18(10), 1091-1095
CODEN: NABIF9; ISSN: 1087-0156

PB Nature America Inc.

DT Journal

LA English

CC 9-15 (Biochemical Methods)

AB Here we describe a new type of **biosensor** element for detecting **proteins** in soln. at nanomolar concns. We tethered a 3.4 kDa polyethylene glycol chain at a defined site within the lumen of the transmembrane **protein pore** formed by **staphylococcal .alpha.-hemolysin**. The free end of the polymer was covalently attached to a biotin mol. On incorporation of the modified **pore** into a lipid bilayer, the biotinyl group moves from one side of the membrane to the other, and is detected by reversible capture with a mutant streptavidin. The capture events are obsd. as changes in ionic current passing through single **pores** in planar bilayers. Accordingly, the modified **pore** allows detection of a **protein** analyte at the single-mol. level, facilitating both quantification and identification through a distinctive current signature. The approach has higher time resolu. compared with other kinetic measurements, such as those obtained by surface plasmon resonance.

ST **protein** detection **hemolysin** polymer chain biotin;
membrane **hemolysin** polymer chain **protein** detection

IT Membrane, biological
(bilayer; detecting **proteins** at nanomolar concns. using **.alpha.-hemolysin** with covalently attached polyethylene glycol and biotin)

IT **Proteins**, specific or class

RL: ANT (Analyte); ANST (Analytical study)
(biotin-binding; detecting **proteins** at nanomolar concns. using **.alpha.-hemolysin** with covalently attached

- polyethylene glycol and biotin)
- IT Polyoxyalkylenes, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (detecting **proteins** at nanomolar concns. using
 .**alpha.-hemolysin** with covalently attached
 polyethylene glycol and biotin)
- IT Electric current
 (ionic, biol.; detecting **proteins** at nanomolar concns. using
 .**alpha.-hemolysin** with covalently attached
 polyethylene glycol and biotin)
- IT **Hemolysins**
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (.**alpha.-**; detecting **proteins** at nanomolar concns.
 using .**alpha.-hemolysin** with covalently attached
 polyethylene glycol and biotin)
- IT 9013-20-1, Streptavidin
 RL: ANT (Analyte); BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); ANST (Analytical study); BIOL
 (Biological study)
 (detecting **proteins** at nanomolar concns. using
 .**alpha.-hemolysin** with covalently attached
 polyethylene glycol and biotin)
- IT 58-85-5, Biotin 25322-68-3, Polyethylene glycol
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (detecting **proteins** at nanomolar concns. using
 .**alpha.-hemolysin** with covalently attached
 polyethylene glycol and biotin)

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE

- (1) Akesson, M; Biophys J 1999, V77, P3227 HCAPLUS
- (2) Bayley, H; Adv Mater 2000, V12, P139 HCAPLUS
- (3) Bezrukov, S; Macromolecules 1996, V29, P8517 HCAPLUS
- (4) Bezrukov, S; Nature 1994, V370, P279 HCAPLUS
- (5) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (6) Chang, C; Chem Biol 1995, V2, P391 HCAPLUS
- (7) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
- (8) Chilkoti, A; Biophys J 1995, V69, P2125 HCAPLUS
- (9) Chilkoti, A; Proc Natl Acad Sci 1995, V92, P1754 HCAPLUS
- (10) Christopher, J; SPOCK: the structural properties observation and
 calculation kit 1998
- (11) Davis, A; Nature 1999, V401, P120 HCAPLUS
- (12) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (13) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (14) Heath, J; Science 1998, V280, P1716 HCAPLUS
- (15) Howorka, S; J Am Chem Soc 2000, V122, P2411 HCAPLUS
- (16) Kasianowicz, J; Proc Natl Acad Sci 1996, V93, P13770 HCAPLUS
- (17) Mao, C; Nature 1999, V397, P144 HCAPLUS
- (18) Marszalek, P; Nature 1999, V402, P100 HCAPLUS
- (19) Mehta, A; Science 1999, V283, P1689 HCAPLUS
- (20) Merzlyak, P; Biophys J 1999, V77, P3023 HCAPLUS
- (21) Montal, M; Proc Natl Acad Sci 1972, V69, P3561 HCAPLUS
- (22) Myszkka, D; J Mol Recognition 1999, V12, P279 HCAPLUS
- (23) Panchal, R; Nat Biotechnol 1996, V14, P852 HCAPLUS
- (24) Perez-Luna, V; J Am Chem Soc 1999, V121, P6469 HCAPLUS
- (25) Russo, M; Nat Biotechnol 1997, V15, P278 HCAPLUS
- (26) Sano, T; Proc Natl Acad Sci 1995, V92, P3180 HCAPLUS
- (27) Seeman, N; Trends Biotechnol 1999, V17, P437 HCAPLUS
- (28) Slatin, S; Nature 1994, V371, P158 HCAPLUS
- (29) Song, L; Science 1996, V274, P1859 HCAPLUS
- (30) Stayton, P; Nature 1995, V378, P472 HCAPLUS
- (31) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS
- (32) Walker, B; J Biol Chem 1995, V270, P23065 HCAPLUS
- (33) Walker, B; Protein Eng 1994, V7, P91 HCAPLUS

- (34) Walker, B; Protein Eng 1995, V8, P491 HCAPLUS
- (35) Weiss, S; Science 1999, V283, P1676 HCAPLUS
- (36) Wong, J; Science 1997, V275, P820 HCAPLUS
- (37) Xie, X; J Biol Chem 1999, V274, P15967 HCAPLUS

L82 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:729252 HCAPLUS

DN 134:52844

TI Interaction of the noncovalent molecular adapter, .beta.-cyclodextrin, with the **staphylococcal .alpha.-hemolysin pore**

AU Gu, Li-Qun; **Bayley, Hagan**

CS Department of Medical Biochemistry and Genetics, The Texas A and M University System Health Science Center, College Station, TX, 77843-1114, USA

SO Biophysical Journal (2000), 79(4), 1967-1975

CODEN: BIOJAU; ISSN: 0006-3495

PB Biophysical Society

DT Journal

LA English

CC 6-3 (General Biochemistry)

AB Cyclodextrins act as noncovalent mol. adapters when lodged in the lumen of the **.alpha.-hemolysin (.alpha.HL) pore**. The adapters act as binding sites for channel blockers,

thereby offering a basis for the detection of a variety of org. mols. with **.alpha.HL** as a **biosensor** element. To further such studies, it is important to find conditions under which the dwell time of cyclodextrins in the lumen of the **pore** is extended. Here, we use single-channel recording to explore the pH- and voltage-dependence of the interaction of .beta.-cyclodextrin (.beta.CD) with **.alpha.HL**. .beta.CD can access its binding site only from the trans entrance of **pores** inserted from the cis side of a bilayer. Anal. of the binding kinetics shows that there is a single binding site for .beta.CD, with an apparent equil. dissocn. const. that varies by >100-fold under the conditions explored. The dissocn. rate const. for the neutral .beta.CD mol. varies with pH and voltage, a result that is incompatible with two states of the **.alpha.HL pore**, one of high and the other of low affinity. Rather, the data suggest that the actual equil. dissocn. const. for the **.alpha.HL .cntdot. .beta.CD** complex varies continuously with the transmembrane potential.

ST **hemolysin alpha pore Staphylococcus**
interaction beta cyclodextrin

IT Membrane, biological

(bilayer; .beta.-cyclodextrin can access its **.alpha.-hemolysin** binding site only from trans entrance of **pores** inserted from cis side of bilayer)

IT Membrane potential

(biol.; equil. dissocn. const. for **.alpha.HL.cntdot..beta.CD** complex varies continuously with transmembrane potential)

IT **Pore**

Staphylococcus aureus

(interaction of .beta.-cyclodextrin with **Staphylococcal .alpha.-hemolysin pore**)

IT **Hemolysins**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**.alpha.-**; interaction of .beta.-cyclodextrin with **Staphylococcal .alpha.-hemolysin pore**)

IT 7585-39-9, .beta.-Cyclodextrin

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(interaction of .beta.-cyclodextrin with **Staphylococcal .alpha.-hemolysin pore**)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Al-yahyaee, S; Bioconjugate Chem 1996, V7, P451 HCAPLUS
- (2) Bayley, H; Adv Mater 2000, V12, P139 HCAPLUS
- (3) Bayley, H; Curr Opin Biotechnol 1999, V10, P94 HCAPLUS
- (4) Bayley, H; Sci Am 1997, V277, P62 HCAPLUS
- (5) Bezrukov, S; Eur Biophys J 1997, V26, P471 HCAPLUS
- (6) Bezrukov, S; J Membr Biol 2000, V174, P1 HCAPLUS
- (7) Bezrukov, S; Phys Rev Lett 1993, V70, P2352 HCAPLUS
- (8) Bhakdi, S; Proc Natl Acad Sci USA 1981, V78, P5475 HCAPLUS
- (9) Botsi, A; Carbohydrate Res 1996, V283, P1 HCAPLUS
- (10) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (11) Chang, C; Chem Biol 1995, V2, P391 HCAPLUS
- (12) Corradini, R; Chem Eur J 1996, V2, P373 HCAPLUS
- (13) D'Souza, V; Chem Rev 1998, V98, P1741 HCAPLUS
- (14) Eroglu, A; Nat Biotechnol 2000, V18, P163 HCAPLUS
- (15) Fussle, R; J Cell Biol 1981, V91, P83 MEDLINE
- (16) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (17) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (18) Gu, L; Proc Natl Acad Sci USA 2000, V97, P3959 HCAPLUS
- (19) Hanke, W; Planar lipid bilayers 1993
- (20) Hille, B; Ionic channels of excitable membranes 1991
- (21) Howorka, S; J Am Chem Soc 2000, V122, P2411 HCAPLUS
- (22) Kasianowicz, J; Biophys J 1995, V69, P94 HCAPLUS
- (23) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (24) Korchew, Y; J Membr Biol 1995, V143, P143 HCAPLUS
- (25) Koshland, D; Biochemistry 1966, V5, P365 HCAPLUS
- (26) Krasilnikov, O; J Membr Biol 1997, V156, P157 HCAPLUS
- (27) Menestrina, G; J Membr Biol 1986, V90, P177 HCAPLUS
- (28) Merzlyak, P; Biophys J 1999, V77, P3023 HCAPLUS
- (29) Moczydlowski, E; Ion Channel Reconstitution 1986, P75
- (30) Montal, M; Proc Natl Acad Sci USA 1972, V69, P3561 HCAPLUS
- (31) Panchal, R; Nat Biotechnol 1996, V14, P852 HCAPLUS
- (32) Pederzolli, C; Bioconjugate Chem 1995, V6, P166 HCAPLUS
- (33) Saenger, W; Chem Rev 1998, V98, P1787 HCAPLUS
- (34) Schneider, H; Chem Rev 1998, V98, P1755 HCAPLUS
- (35) Song, L; Science 1996, V274, P1859 HCAPLUS
- (36) Szejtli, J; Chem Rev 1998, V98, P1743 HCAPLUS
- (37) Walker, B; Chem Biol 1995, V2, P99 HCAPLUS
- (38) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS
- (39) Woodhull, A; J Gen Physiol 1973, V61, P687 HCAPLUS
- (40) Ziegler, C; Curr Opin Chem Biol 1998, V2, P585 HCAPLUS

L82 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:628848 HCAPLUS

DN 133:346704

TI Simultaneous stochastic sensing of divalent metal ions

AU Braha, Orit; Gu, Lin-Qun; Zhou, Li; Lu, Xiaofeng; Cheley, Stephen;

Bayley, Hagan

CS Department of Medical Biochemistry and Genetics, The Texas A and M University System Health Science Center, College Station, TX, 77843-1114, USA

SO Nat. Biotechnol. (2000), 18(9), 1005-1007

CODEN: NABIF9; ISSN: 1087-0156

PB Nature America Inc.

DT Journal

LA English

CC 9-16 (Biochemical Methods)

AB Stochastic sensing is an emerging anal. technique that relies upon single-mol. detection. Transmembrane **pores**, into which binding sites for analytes have been placed by genetic engineering, have been developed as stochastic sensing elements. Reversible occupation of an engineered binding site modulates the ionic current passing through a **pore** in a transmembrane potential and thereby provides both the concn. of an analyte and, through a characteristic signature, its identity. Here, we show that the concns. of two or more divalent metal ions in soln. can be detd. simultaneously with a single **sensor** element. Further, the **sensor** element can be permanently

calibrated without a detailed understanding of the kinetics of interaction of the metal ions with the engineered **pore**.

ST stochastic sensing divalent metal ion

IT **Pore**
(Transmembrane; simultaneous stochastic sensing of divalent metal ions)

IT Ion channel
RL: ANT (Analyte); ANST (Analytical study)
(Transmembrane; simultaneous stochastic sensing of divalent metal ions)

IT Cations
(divalent; simultaneous stochastic sensing of divalent metal ions)

IT **Hemolysins**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(.alpha.-; simultaneous stochastic sensing of divalent metal ions)

IT 15158-11-9, analysis 22537-48-0, Cadmium ion, analysis 23713-49-7, Zinc ion, analysis
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous stochastic sensing of divalent metal ions)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bayley, H; Adv Mater 2000, V12, P139 HCAPLUS
- (2) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (3) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (4) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (5) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (6) Hanke, W; Planar lipid bilayers 1993
- (7) Hume, R; Nature 1983, V305, P632 HCAPLUS
- (8) Kasianowicz, J; Biophys J 1999, V76, P837 HCAPLUS
- (9) Kramer, R; Neuron 1990, V4, P335 HCAPLUS
- (10) Motesharei, K; J Am Chem Soc 1997, V119, P11306 HCAPLUS
- (11) Olson, R; Nat Struct Biol 1999, V6, P134 HCAPLUS
- (12) Pedelacq, J; Structure 1999, V7, P277 HCAPLUS
- (13) Proakis, J; Digital signal processing: principles, algorithms and applications 1995
- (14) Qin, F; www.qub.buffalo.edu
- (15) Song, L; Science 1996, V274, P1859 HCAPLUS
- (16) Vivaudou, M; J Membrane Biol 1991, V122, P165 HCAPLUS
- (17) Young, S; Nature 1983, V305, P634 HCAPLUS

L82 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:410575 HCAPLUS

DN 133:189996

TI Resistive-Pulse Sensing-From Microbes to Molecules

AU **Bayley, Hagan**; Martin, Charles R.

CS Department of Medical Biochemistry and Genetics, Texas A&M University System Health Science Center, College Station, TX, 77843-1114, USA

SO Chem. Rev. (Washington, D. C.) (2000), 100(7), 2575-2594
CODEN: CHREAY; ISSN: 0009-2665

PB American Chemical Society

DT Journal; General Review

LA English

CC 9-0 (Biochemical Methods)

AB A review with 173 refs. In this review we attempted to unify various apparently disparate sensing strategies. The unifying feature is the underlying measurement principle which entails occlusions of an aperture through which a current is passing by the analyte species. While we began with a classical and a com. available device, the review focused on two very recent manifestations of this sensing paradigm-the use of **protein**-based channels and nanotube membranes for small mol. and ion sensing.

ST review pulse sensing microbe mol

IT Membrane, biological
Nanotubes
Sensors
(resistive-pulse sensing-from microbes to mols.)

IT Ion channel

Proteins, general, properties

RL: PEP (Physical, engineering or chemical process); PRP (Properties);
PROC (Process)

(resistive-pulse sensing-from microbes to mols.)

RE.CNT 173 THERE ARE 173 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Akerfeldt, K; Acc Chem Res 1993, V26, P191 HCAPLUS
- (2) Akeson, M; Biophys J 1999, V77, P3227 HCAPLUS
- (3) Allen, T; Trends Neurosci 1997, V20, P192 HCAPLUS
- (4) Alper, J; Science 1999, V284, P1754 HCAPLUS
- (5) Andersen, C; J Gen Physiol 1995, V105, P385 HCAPLUS
- (6) Andersen, C; J Membr Biol 1998, V164, P263 HCAPLUS
- (7) Anderson, O; Biophys J 1999, V77, P2899
- (8) Anon; Personal communication from Rick Shimkus Micromeritics, Inc 1999
- (9) Anon; www.beckman.com/coulter/PC/SS000091.ASP
- (10) Anon; www.micromeritics.com/ps_elzone.html
- (11) Arkin, I; EMBO J 1994, V13, P4757 HCAPLUS
- (12) Armstrong, C; Neuron 1998, V20, P371 HCAPLUS
- (13) Baltzer, L; Curr Opin Struct Biol 1998, V8, P466 HCAPLUS
- (14) Bayley, H; Curr Opin Biotechnol 1999, V10, P94 HCAPLUS
- (15) Bean, R; J Gen Physiol 1969, V53, P741 HCAPLUS
- (16) Benson, D; Curr Opin Biotechnol 1998, V9, P370 HCAPLUS
- (17) Bezrukov, S; Biophys J 1993, V64, P16 HCAPLUS
- (18) Bezrukov, S; Eur Biophys J 1997, V26, P471 HCAPLUS
- (19) Bezrukov, S; Macromolecules 1996, V29, P8517 HCAPLUS
- (20) Bezrukov, S; Nature 1994, V370, P279 HCAPLUS
- (21) Bezrukov, S; Phys Rev Lett 1993, V70, P2352 HCAPLUS
- (22) Bhakdi, S; Arch Microbiol 1996, V165, P73 HCAPLUS
- (23) Bhakdi, S; Infect Immunol 1984, V46, P318 HCAPLUS
- (24) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (25) Buchanan, S; Nature Struct Biol 1999, V6, P56 HCAPLUS
- (26) Chang, G; Science 1998, V282, P2220 HCAPLUS
- (27) Che, G; Langmuir 1999, V15, P750 HCAPLUS
- (28) Che, G; Nature 1998, V398, P346
- (29) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
- (30) Church, G; US 5795782 1998
- (31) Clark, T; J Am Chem Soc 1998, V120, P651 HCAPLUS
- (32) Corey, D; Biochemistry 1989, V28, P8277 HCAPLUS
- (33) Corey, D; Science 1987, V238, P1401 HCAPLUS
- (34) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (35) Coronado, R; Biophys J 1983, V43, P231 HCAPLUS
- (36) Deblois, R; J Virol 1977, V23, P227 MEDLINE
- (37) Deblois, R; Rev Sci Instrum 1970, V41, P909
- (38) Deen, V; AIChEJ 1987, V33, P14091425
- (39) Defelice, L; Introduction to membrane noise 1981
- (40) Degrado, W; Science 1997, V278, P80 HCAPLUS
- (41) Dehiyat, B; Science 1997, V278, P82
- (42) Dieckmann, G; Curr Opin Struct Biol 1997, V7, P486 HCAPLUS
- (43) Dingleline, R; Pharmacol Rev 1999, V51 HCAPLUS
- (44) Distefano, M; Curr Opin Struct Biol 1998, V8, P459 HCAPLUS
- (45) Doyle, D; Science 1998, V280, P69 HCAPLUS
- (46) Dutzler, R; Structure 1996, V3, P127
- (47) D'Souza, V; Chem Rev 1998, V98(5 special issue)
- (48) Elling, C; Fold Des 1997, V2, P576 HCAPLUS
- (49) Elling, C; Nature 1995, V374, P74 HCAPLUS
- (50) England, P; Cell 1999, V96, P89 HCAPLUS
- (51) England, P; Proc Natl Acad Sci U S A 1997, V94, P11025 HCAPLUS
- (52) Ferguson, A; Science 1998, V282, P2215 HCAPLUS
- (53) Fishman, H; Annu Rev Biophys Biomol Struct 1998, V27, P165 HCAPLUS
- (54) Fleischer, R; Nuclear Tracks in Solids 1975
- (55) Fleming, K; J Mol Biol 1997, V272, P266 HCAPLUS
- (56) Forman, S; Biophys J 1997, V72, P2170 HCAPLUS
- (57) Forman, S; Mol Pharmacol 1995, V48, P574 HCAPLUS
- (58) Fukushima, Y; J Physiol 1982, V331, P311 HCAPLUS
- (59) Fussle, R; J Cell Biol 1981, V91, P83 MEDLINE
- (60) Futaki, S; Tetrahedron Lett 1997, V38, P7071 HCAPLUS

- (61) Gallivan, J; Chem Biol 1997, V4, P739 HCAPLUS
- (62) Ghadiril, M; Nature 1994, V369, P301 HCAPLUS
- (63) Gouaux, E; Curr Opin Struct Biol 1997, V7, P566 HCAPLUS
- (64) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (65) Gouaux, J; Proc Natl Acad Sci U S A 1994, V91, P12828 HCAPLUS
- (66) Griffin, B; Science 1998, V281, P269 HCAPLUS
- (67) Gritsch, S; Langmuir 1998, V14, P3118 HCAPLUS
- (68) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (69) Hamachi, I; Bioconjugate Chem 1997, V8, P862 HCAPLUS
- (70) Hamill, O; Pflgers Arch 1981, V391, P85 MEDLINE
- (71) Hanke, W; Planar lipid bilayers 1993
- (72) Hartgerink, J; Chem Eur J 1998, V4, P1367 HCAPLUS
- (73) Heinemann, S; Biochim Biophys Acta 1989, V987, P8 HCAPLUS
- (74) Heyse, S; Biochim Biophys Acta 1998, V1376, P319 HCAPLUS
- (75) Hille, B; Ionic channels of excitable membranes 1991
- (76) Hladky, S; Nature 1970, V225, P451 HCAPLUS
- (77) Hulteen, J; J Am Chem Soc 1998, V120, P6603 HCAPLUS
- (78) Hulteen, J; J Mater Chem 1997, V7, P1075 HCAPLUS
- (79) Hume, R; Nature 1983, V305, P632 HCAPLUS
- (80) Hwa, I; Int J Mol Med 1999, V4, P175 MEDLINE
- (81) Jardemark, K; Anal Chem 1997, V69, P3427 HCAPLUS
- (82) Jardemark, K; Anal Chem 1998, V70, P2468 HCAPLUS
- (83) Jirage, K; Anal Chem 1999, V71, P4913 HCAPLUS
- (84) Jirage, K; Science 1997, V278, P655 HCAPLUS
- (85) Karlin, A; Neuron 1995, V15, P1227
- (86) Kasianowicz, J; Biophys J 1999, V76, P837 HCAPLUS
- (87) Kasianowicz, J; Proc Natl Acad Sci U S A 1996, V93, P13770 HCAPLUS
- (88) Kathawalla, I; Macromolecules 1989, V22, P1215 HCAPLUS
- (89) Kearney, P; Neuron 1996, V17, P1221 HCAPLUS
- (90) Kobayashi, Y; Anal Chem 1999, V71, P3665 HCAPLUS
- (91) Kobayashi, Y; J Electroanal Chem 1997, V431, P29 HCAPLUS
- (92) Koch, M; J Micromech Microeng 1999, V9, P159 HCAPLUS
- (93) Kramer, R; Neuron 1990, V4, P335 HCAPLUS
- (94) Krasilnikov, O; FEMS Microbiol Immunol 1992, V105, P93
- (95) Kubitschek, H; Methods in Microbiology
- (96) Lear, J; J Am Chem Soc 1997, V119, P3212 HCAPLUS
- (97) Lehn, J; Comprehensive supramolecular chemistry 1997
- (98) Lehn, J; Supramolecular chemistry: concepts and perspectives 1995
- (99) Liman, E; Neuron 1992, V9, P861 HCAPLUS
- (100) Lindemann, B; Science 1977, V195, P292 HCAPLUS
- (101) Lines, R; Particle Size Analysis,
- (102) Locher, K; Cell 1998, V95, P771 HCAPLUS
- (103) Lu, H; Science 1998, V282, P1877 HCAPLUS
- (104) Lu, Q; Science 1995, V268, P304 HCAPLUS
- (105) Lubensky, D; Biophys J 1999, V77, P1824 HCAPLUS
- (106) Mackenzie, K; Proc Natl Acad Sci U S A 1998, V95, P3583 HCAPLUS
- (107) Martin, C; J Electroanal Chem 1983, V115, P267
- (108) Martin, C; Science 1994, V266, P1961 HCAPLUS
- (109) Mehta, A; Science 1999, V283, P1689 HCAPLUS
- (110) Meller, A; Proc Natl Acad Sci U S A 2000, V97, P1079 HCAPLUS
- (111) Menestrina, G; J Membr Biol 1986, V90, P177 HCAPLUS
- (112) Menon, V; Anal Chem 1995, V67, P1920 HCAPLUS
- (113) Merzlyak, P; Biophys J 1999, V77, P3023 HCAPLUS
- (114) Miller, J; Neuron 1998, V20, P619 HCAPLUS
- (115) Montal, M; Curr Opin Struct Biol 1995, V5, P501 HCAPLUS
- (116) Montal, M; FEBS Lett 1993, V320, P261 HCAPLUS
- (117) Mueller, P; J Theor Biol 1968, V18, P222 HCAPLUS
- (118) Mueller, P; Nature 1962, V194, P979 HCAPLUS
- (119) Neher, E; Annu Rev Biophys Bioeng 1977, V6, P345 HCAPLUS
- (120) Neher, E; J Physiol 1978, V277, P153 HCAPLUS
- (121) Neher, E; Nature 1976, V260, P779
- (122) Nekolla, S; Biophys J 1994, V66, P1388 HCAPLUS
- (123) Nishizawa, M; Science 1995, V268, P700 HCAPLUS
- (124) Nitsche, J; Ind Eng Chem Res 1994, V33, P2242 HCAPLUS
- (125) Nowak, M; Science 1995, V268, P439 HCAPLUS
- (126) Oberhauser, A; Nature 1998, V393, P181 HCAPLUS

- (127) Olson, R; Nature Struct Biol 1999, V6, P134 HCAPLUS
- (128) Orwar, O; Methods Enzymol 1999, V294, P189 HCAPLUS
- (129) Orwar, O; Science 1996, V272, P1779 HCAPLUS
- (130) Pautsch, A; Nature Struct Biol 1998, V5, P1013 HCAPLUS
- (131) Pawlak, M; Protein Sci 1994, V3, P1788 HCAPLUS
- (132) Pedelacq, J; Structure 1999, V7, P277 HCAPLUS
- (133) Pei, D; Proc Natl Acad Sci U S A 1990, V87, P9858 HCAPLUS
- (134) Petzny, W; Science 1969, V166, P751 HCAPLUS
- (135) Prat, Z; J Electroanal Chem 1991, V315, P225
- (136) Preston, G; J Biol Chem 1993, V268, P17 HCAPLUS
- (137) Raguse, B; Langmuir 1998, V14, P648 HCAPLUS
- (138) Ramon, R; Trans R Soc Trop Med Hyg 1999, V93, P419 MEDLINE
- (139) Rekharsky, M; Chem Rev 1998, V98, P1875 HCAPLUS
- (140) Rief, M; Science 1997, V276, P1109 HCAPLUS
- (141) Rostovtseva, T; Biophys J 1998, V74, P2365 HCAPLUS
- (142) Rostovtseva, T; J Membr Biol 1996, V151, P29 HCAPLUS
- (143) Sackmann, E; Science 1996, V271, P43 HCAPLUS
- (144) Sansom, M; Curr Biol 1999, V9, PR254 HCAPLUS
- (145) Schirmer, T; Science 1995, V267, P512 HCAPLUS
- (146) Schulz, G; Curr Opin Struct Biol 1996, V6, P485 HCAPLUS
- (147) Schuster, B; Biochim Biophys Acta 1998, V1370, P280 HCAPLUS
- (148) Schuster, B; Biochim Biophys Acta 1998, V1369, P51 HCAPLUS
- (149) Shear, J; Science 1995, V267, P74 HCAPLUS
- (150) Smithrud, D; Curr Opin Biotechnol 1997, V8, P459 HCAPLUS
- (151) Song, L; Science 1996, V274, P1859 HCAPLUS
- (152) Stora, T; Angew Chem, Int Ed Engl 1999, V38, P389 HCAPLUS
- (153) Suarez-Isla, B; Biochemistry 1983, V22, P2319 HCAPLUS
- (154) Sun, L; Langmuir 1999, V15, P738 HCAPLUS
- (155) Trivedi, B; Neuron 1998, V21, P895 HCAPLUS
- (156) Trivedi, B; Neuron, in press
- (157) Valeva, A; EMBO J 1996, V15, P1857 HCAPLUS
- (158) van Driessche, W; Noise and Impedance Analysis 1994, P27
- (159) Vodyanoy, I; Biophys J 1992, V62, P10 HCAPLUS
- (160) Wade, H; Annu Rev Biophys Biomol Struct 1997, V26, P461 HCAPLUS
- (161) Walker, B; Chem Biol 1995, V2, P99 HCAPLUS
- (162) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS
- (163) Walker, B; Protein Eng 1994, V7, P655 HCAPLUS
- (164) Walker, B; Protein Eng 1995, V8, P491 HCAPLUS
- (165) Weiss, S; Science 1999, V283, P1676 HCAPLUS
- (166) Wentworth, P; Curr Opin Chem Biol 1998, V2, P138 HCAPLUS
- (167) Woodhull, A; J Gen Physiol 1973, V61, P687 HCAPLUS
- (168) Xie, X; J Biol Chem 1999, V274, P15967 HCAPLUS
- (169) Yang, J; Neuron 1995, V15, P1441 HCAPLUS
- (170) Yellen, G; Rev Biophys 1998, V31, P239 HCAPLUS
- (171) Young, S; Nature 1983, V305, P634 HCAPLUS
- (172) Zimmerberg, J; Nature 1986, V323, P36 HCAPLUS
- (173) Zuckermann, R; Proc Natl Acad Sci U S A 1989, V86, P1766 HCAPLUS

L82 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:213198 HCAPLUS

DN 132:326109

TI Stochastic sensing of organic analytes by a pore-forming
protein containing a molecular adapter

AU Schultzberg, Maria; Boulin, Christian; Dandekar, Thomas
CS European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
SO Chemtracts (2000), 13(3), 198-202

CODEN: CHEMFW; ISSN: 1431-9268

PB Springer-Verlag New York Inc.

DT Journal; General Review

LA English

CC 64-1 (Pharmaceutical Analysis)

Section cross-reference(s): 9

AB The title research of Li-Qun Gu, et al. (1999) is reviewed with
commentary; 15 refs.

ST review hemolysin biosensor; hemolysin biosensor
review; biosensor hemolysin review

IT **Biosensors**

(stochastic sensing of org. analytes by a **pore-forming protein** contg. mol. adapter)

IT **Hemolysins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.-; stochastic sensing of org. analytes by a **pore-forming protein** contg. mol. adapter)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Bayley, H; Curr Opin Biotech 1999, V10, P94 HCAPLUS
- (2) Bayley, H; Sci Am 1997, V277, P62 HCAPLUS
- (3) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (4) Chang, C; Chem Biol 1995, V2, P391 HCAPLUS
- (5) Clark, L; Ann NY Acad Sci 1962, V148, P133
- (6) Costello, R; Biosens Bioel 1999, V14, P265 HCAPLUS
- (7) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (8) Harris, B; Trends Biotech 1999, V17, P290 HCAPLUS
- (9) Hartgerink, J; Chem Eur J 1998, V4, P1367 HCAPLUS
- (10) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (11) Montal, M; Proc Natl Acad Sci USA 1972, V69, P3561 HCAPLUS
- (12) Rekharsky, M; Chem Rev 1998, V98, P1875 HCAPLUS
- (13) Schuster, B; Biochim Biophys Acta 1998, V1370, P280 HCAPLUS
- (14) Song, L; Science 1996, V274, P1859 HCAPLUS
- (15) Walker, B; Protein Eng 1994, V7, P655 HCAPLUS

L82 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:136032 HCAPLUS

DN 132:276277

TI A **Protein Pore** with a Single Polymer Chain Tethered within the Lumen

AU **Howorka, Stefan; Movileanu, Liviu; Lu, Xiaofeng;**

Magnon, Melissa; Cheley, Stephen; Braha, Orit; **Bayley, Hagan**
CS Department of Medical Biochemistry & Genetics, Texas A&M Health Science Center, College Station, TX, 77843-1114, USA

SO J. Am. Chem. Soc. (2000), 122(11), 2411-2416
CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

CC 9-16 (Biochemical Methods)

AB A transmembrane **protein pore** with a single 5000 Da poly(ethylene glycol) (PEG) mol. attached covalently within the channel lumen has been constructed from seven **staphylococcal .alpha.-hemolysin** subunits. The modified heptamer is stable and can be purified by electrophoresis in sodium dodecyl sulfate, without disson. of the subunits. The properties of the modified **pore** were studied by single channel current recording. The PEG mol. reduces the mean conductance of the **pore** by 18%, as would be predicted from the effects of PEG on the cond. of bulk electrolytes. The recordings also reveal a variety of low amplitude current fluctuations on a time scale of seconds, which are tentatively ascribed to the reorganization of the PEG mol. within the channel lumen and assocd. movements of the **polypeptide** chain. Another class of events, comprising uniform high-amplitude neg. fluctuations in current with durations of milliseconds, is ascribed to motions of the PEG mol. into one of the channel entrances, thereby producing more extensive channel block. When instead a 3000 Da PEG is attached within the channel lumen, the single channel properties are changed in keeping with the lower mass of the polymer. For example, the high-amplitude fluctuations occur more frequently and are of shorter duration suggesting that the 3000 Da PEG is more mobile than the 5000 Da chain. With further development, the approach taken here should be useful for the indirect monitoring of polymer dynamics at the single mol. level. By using polymers that respond to analytes, it should also be possible to make **biosensors** from the covalently modified **pores**.

ST **protein pore** engineering lumen PEG chain; polyethylene

- glycol **protein pore**
- IT Electric conductivity
Electric current
(biol.; heptameric transmembrane **protein pore**
constructed with **hemolysin** subunits and contains
poly(ethylene glycol) chain tethered to **pore** lumen)
- IT Electrolytes, biological
(heptameric transmembrane **protein pore** constructed
with **hemolysin** subunits and contains poly(ethylene glycol)
chain tethered to **pore** lumen)
- IT Polyoxyalkylenes, biological studies
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(heptameric transmembrane **protein pore** constructed
with **hemolysin** subunits and contains poly(ethylene glycol)
chain tethered to **pore** lumen)
- IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(transmembrane, **pore**; heptameric transmembrane
protein pore constructed with **hemolysin**
subunits and contains poly(ethylene glycol) chain tethered to
pore lumen)
- IT **Hemolysins**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(.alpha.-; heptameric transmembrane **protein**
pore constructed with **hemolysin** subunits and contains
poly(ethylene glycol) chain tethered to **pore** lumen)
- IT 25322-68-3, Poly(ethylene glycol)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(heptameric transmembrane **protein pore** constructed
with **hemolysin** subunits and contains poly(ethylene glycol)
chain tethered to **pore** lumen)

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bayley, H; Adv Mater in press 2000
- (2) Bayley, H; Chem Rev in press 2000
- (3) Bayley, H; Curr Op Biotechnol 1999, V10, P94 HCAPLUS
- (4) Bezrukov, S; Biophys J 1993, V64, P16 HCAPLUS
- (5) Bezrukov, S; Eur Biophys J 1997, V26, P471 HCAPLUS
- (6) Bezrukov, S; Macromolecules 1996, V29, P8517 HCAPLUS
- (7) Bezrukov, S; Nature 1994, V370, P279 HCAPLUS
- (8) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (9) Chang, C; Chem Biol 1995, V2, P391 HCAPLUS
- (10) Cheley, S; Protein Sci 1999, V8, P1257 HCAPLUS
- (11) Ding, Z; Bioconjugate Chem 1999, V10, P395 HCAPLUS
- (12) Doi, M; Introduction to polymer physics 1996
- (13) Fussle, R; J Cell Biol 1981, V91, P83 MEDLINE
- (14) Gimzewski, J; Science 1999, V283, P1683 HCAPLUS
- (15) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (16) Ha, T; Proc Natl Acad Sci U S A 1999, V96, P893 HCAPLUS
- (17) Hladky, S; Nature 1970, V225, P451 HCAPLUS
- (18) Hoffman, A; Macromol Symp 1995, V98, P645 HCAPLUS
- (19) Hubbell, J; Curr Op Biotechnol 1999, V10, P123 HCAPLUS
- (20) Kay, L; Nature Struct Biol 1998, V5, P145
- (21) Kenworthy, A; Biophys J 1995, V68, P1921 HCAPLUS
- (22) Krasilnikov, O; FEMS Microbiol Immunol 1992, V105, P93
- (23) Lu, H; Science 1998, V282, P1877 HCAPLUS
- (24) Mehta, A; Science 1999, V283, P1689 HCAPLUS
- (25) Menestrina, G; J Membr Biol 1986, V90, P177 HCAPLUS
- (26) Moerner, W; Science 1999, V283, P1670 HCAPLUS
- (27) Montal, M; Proc Natl Acad Sci U S A 1972, V69, P3561 HCAPLUS
- (28) Olson, R; Nature Struct Biol 1999, V6, P134 HCAPLUS
- (29) Rex, S; Biophys J 1998, V75, P2900 HCAPLUS

- (30) Sakmann, B; Single-channel recording 1995
 (31) Scherrer, R; J Bacteriol 1971, V107, P718 HCAPLUS
 (32) Sheth, S; Proc Natl Acad Sci U S A 1997, V94, P8399 HCAPLUS
 (33) Song, I; Science 1996, V274, P1859
 (34) Stayton, P; Nature 1995, V378, P472 HCAPLUS
 (35) Tan, W; Anal Chem 1997, V69, P4242 HCAPLUS
 (36) Urry, D; Biopolymers 1998, V47, P167 HCAPLUS
 (37) Walker, B; Chem Biol 1995, V2, P99 HCAPLUS
 (38) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS
 (39) Walker, B; J Biol Chem 1992, V267, P21782 HCAPLUS
 (40) Walker, B; J Biol Chem 1993, V268, P5285 HCAPLUS
 (41) Walker, B; J Biol Chem 1995, V270, P23065 HCAPLUS
 (42) Walker, B; Protein Eng 1995, V8, P491 HCAPLUS
 (43) Walker, B; Protein Eng 1994, V7, P91 HCAPLUS
 (44) Weiss, S; Science 1999, V283, P1676 HCAPLUS
 (45) Wong, J; Science 1997, V275, P820 HCAPLUS
 (46) Xie, X; J Biol Chem 1999, V274, P15967 HCAPLUS
 (47) Xue, Q; Nature 1995, V373, P681 HCAPLUS
 (48) Ziegler, C; Curr Op Chem Biol 1998, V2, P585 HCAPLUS
- L82 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:62780 HCAPLUS
 DN 132:104791
 TI Stochastic sensing with **protein pores**
 AU **Bayley, Hagan**; Braha, Orit; Gu, Li-Qun
 CS Dep. Medical Biochem. Genetics, Texas A & M Health Science Center, College Station, TX, 77843, USA
 SO Adv. Mater. (Weinheim, Ger.) (2000), 12(2), 139-142
 CODEN: ADVMEW; ISSN: 0935-9648
 PB Wiley-VCH Verlag GmbH
 DT Journal; General Review
 LA English
 CC 9-0 (Biochemical Methods)
 AB A review with 28 refs. is given on the use of engineered transmembrane **protein pores** as stochastic **biosensor** elements including natural ion channels as **sensors**, and the genetically engineered **staphylococcal .alpha.-hemolysin** for the detection of metals and with a cyclodextrin-modified **protein pore** for the detection of org. mols.
 ST review **biosensor protein pore** metal detn;
 org substance **biosensor protein pore** review;
 ion channel **biosensor** review
 IT **Proteins**, general, analysis
 RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
 (cyclodextrin-modified; stochastic sensing with **protein pores**)
 IT **Biosensors**
 (stochastic sensing with **protein pores**)
 IT Metals, analysis
 Organic compounds, analysis
 RL: ANT (Analyte); ANST (Analytical study)
 (stochastic sensing with **protein pores**)
 IT Ion channel
 RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
 (stochastic sensing with **protein pores**)
 IT **Hemolysins**
 RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
 (.alpha.-, bacterial; stochastic sensing with **protein pores**)
- RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE
 (1) Allen, T; Trends Neurosci 1997, V20, P192 HCAPLUS
 (2) Bayley, H; Curr Opin Biotechnol 1999, V10, P94 HCAPLUS

- (3) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (4) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (5) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (6) Gu, L; Nature 1999, V398, P686 HCAPLUS
- (7) Gu, L; unpublished
- (8) Hellinga, H; Trends Biotechnol 1998, V16, P183 HCAPLUS
- (9) Heyse, S; Biochim Biophys Acta 1998, V1376, P319 HCAPLUS
- (10) Hulteen, J; J Am Chem Soc 1998, V120, P6603 HCAPLUS
- (11) Hume, R; Nature 1983, V305, P632 HCAPLUS
- (12) Kasianowicz, J; Biophys J 1999, V76, P837 HCAPLUS
- (13) Kramer, R; Neuron 1990, V4, P335 HCAPLUS
- (14) Lowe, C; Curr Opin Chem Biol 1999, V3, P106 HCAPLUS
- (15) Menestrina, G; J Membr Biol 1986, V90, P177 HCAPLUS
- (16) Orwar, O; Methods Enzymol 1999, V294, P189 HCAPLUS
- (17) Sackmann, E; Science 1996, V271, P43 HCAPLUS
- (18) Schuster, B; Biochim Biophys Acta 1998, V1370, P280 HCAPLUS
- (19) Shear, J; Science 1995, V267, P74 HCAPLUS
- (20) Song, L; Science 1996, V274, P1859 HCAPLUS
- (21) Stora, T; Angew Chem Int Ed 1999, V38, P389 HCAPLUS
- (22) Sun, L; Langmuir 1999, V15, P738 HCAPLUS
- (23) Trivedi, B; Neuron 1998, V21, P895 HCAPLUS
- (24) Walker, B; Protein Eng 1994, V7, P655 HCAPLUS
- (25) Weiss, S; Science 1999, V283, P1676 HCAPLUS
- (26) Xie, X; J Biol Chem 1999, V274, P15967 HCAPLUS
- (27) Young, S; Nature 1983, V305, P634 HCAPLUS
- (28) Ziegler, C; Curr Opin Chem Biol 1998, V2, P585 HCAPLUS

L82 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:283318 HCAPLUS

DN 131:92613

TI Stochastic sensing of organic analytes by a **pore**-forming
protein containing a molecular adapter

AU Gu, Li-Qun; Braha, Orit; Conlan, Sean; Cheley, Stephen; **Bayley,**
Hagan

CS Department of Medical Biochemistry & Genetics, Texas A&M University Health
Science Center, College Station, TX, 77843-1114, USA

SO Nature (London) (1999), 398(6729), 686-690
CODEN: NATUAS; ISSN: 0028-0836

PB Macmillan Magazines

DT Journal

LA English

CC 64-3 (Pharmaceutical Analysis)

AB The detection of org. mols. is important in many areas, including
medicine, environmental monitoring and defense. Stochastic sensing is an
approach that relies on the observation of individual binding events
between analyte mols. and a single receptor. Engineered transmembrane
protein pores are promising **sensor** elements
for stochastic detection, and in their simplest manifestation they produce
a fluctuating binary ('on/off') response in the transmembrane elec.
current. The frequency of occurrence of the fluctuations reveals the
concn. of the analyte, and its identity can be deduced from the
characteristic magnitude and/or duration of the fluctuations. Genetically
engineered versions of the bacterial **pore**-forming
protein .alpha.-hemolysin have been used to
identify the quantify divalent metal ions in soln. But it is not
immediately obvious how versatile binding sites for org. ligands might be
obtained by engineering of the **pore** structure. Here we show
that stochastic sensing of org. mols. can be procured from **.alpha**
.-hemolysin by equipping the channel with an internal,
non-covalently bound mol. 'adapter' which mediates channel blocking by the
analyte. We use cyclodextrins as the adapters because these fit
comfortably inside the **pore** and present a hydrophobic cavity
suitable for binding a variety of org. analytes. Moreover, a single
sensing element of this sort can be used to analyze a mixt. of org. mols.
with different binding characteristics. We envisage the use of other
adapters, so that the **pore** could be 'programmed' for a range of

sensing functions.

ST **hemolysin** cyclodextrin adapter **biosensor** org compd;
drug analysis **biosensor hemolysin** cyclodextrin

IT **Biosensors**
Pharmaceutical analysis
(stochastic sensing of org. analytes by **pore**-forming
.alpha.-hemolysin contg. cyclodextrin as mol.
adapter)

IT **Hemolysins**
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(**.alpha.-**; stochastic sensing of org. analytes by
pore-forming **.alpha.-hemolysin** contg.
cyclodextrin as mol. adapter)

IT 50-49-7, Imipramine 60-87-7, Promethazine 828-51-3,
1-Adamantanecarboxylic acid 13074-39-0, 2-Adamantanamine
RL: ANT (Analyte); ANST (Analytical study)
(stochastic sensing of org. analytes by **pore**-forming
.alpha.-hemolysin contg. cyclodextrin as mol.
adapter)

IT 7585-39-9, **.beta.-Cyclodextrin** 12619-70-4, Cyclodextrin
RL: ARU (Analytical role, unclassified); MOA (Modifier or additive use);
ANST (Analytical study); USES (Uses)
(stochastic sensing of org. analytes by **pore**-forming
.alpha.-hemolysin contg. cyclodextrin as mol.
adapter)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Arduini, A; Curr Opin Chem Biol 1997, V1, P467 HCAPLUS
- (2) Bayley, H; Sci Am 1997, V277(Sept), P62
- (3) Beer, P; Curr Opin Chem Biol 1997, V1, P475 HCAPLUS
- (4) Bezrukov, S; Macromolecules 1996, V29, P8517 HCAPLUS
- (5) Bhakdi, S; Proc Natl Acad Sci USA 1981, V78, P5475 HCAPLUS
- (6) Bianchet, M; Nature Struct Biol 1996, V3, P934 MEDLINE
- (7) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (8) Chen, H; Curr Opin Chem Biol 1997, V1, P458 HCAPLUS
- (9) Christopher, J; SPOCK: The Structural Properties and Calculation Kit
(Program Manual) 1998
- (10) Colquhoun, D; Phil Trans R Soc Lond B 1982, V300, P1 MEDLINE
- (11) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (12) Crooks, R; Acc Chem Res 1998, V31, P199
- (13) Czarnik, A; Nature 1998, V394, P417 HCAPLUS
- (14) Dickinson, T; Nature 1996, V382, P687
- (15) Gouaux, E; J Struct Biol 1998, V121, P110 HCAPLUS
- (16) Hartgerink, J; Chem Eur J 1998, V4, P1367 HCAPLUS
- (17) Hellinga, H; Trends Biotechnol 1998, V16, P183 HCAPLUS
- (18) Inoue, Y; J Am Chem Soc 1993, V115, P475 HCAPLUS
- (19) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (20) Krasilnikov, O; FEMS Microbiol Immunol 1992, V105, P93
- (21) Lonergan, M; Chem Mat 1996, V8, P2298 HCAPLUS
- (22) Lu, H; Science 1998, V282, P1877 HCAPLUS
- (23) Lucchesi, K; J Membr Biol 1989, V109, P269 HCAPLUS
- (24) Montal, M; Proc Natl Acad Sci USA 1972, V69, P3561 HCAPLUS
- (25) Oberhauser, A; Nature 1998, V393, P181 HCAPLUS
- (26) Rekharsky, M; Chem Rev 1998, V98, P1875 HCAPLUS
- (27) Schmid, B; Protein Sci 1998, V7, P1603 HCAPLUS
- (28) Song, L; Science 1996, V274, P1859 HCAPLUS
- (29) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS

L82 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:124048 HCAPLUS

DN 130:293399

TI Designed membrane channels and **pores**

AU **Bayley, Hagan**

CS Department of Medical Biochemistry and Genetics, Texas AandM Health
Science Center, College Station, TX, 77843-1114, USA

SO Curr. Opin. Biotechnol. (1999), 10(1), 94-103

CODEN: CUOBE3; ISSN: 0958-1669

PB Current Biology Publications

DT Journal; General Review

LA English

CC 9-0 (Biochemical Methods)

AB A review with 72 refs. Advances in the synthesis and assembly of designed membrane channels and **pores** include addressable template-assisted synthetic **protein** (TASP) syntheses of helix bundles, the prodn. of a new class of nanotubes and the ability to purify hetero-oligomeric **pores**. Channels and **pores** with altered functional properties and with built-in triggers and switches have been prepd. Progress in applications has been greatest in **sensor** technol., where **sensor** elements based on ligand activation, channel selectivity and channel block have been made. Structural information about natural membrane **proteins** is emerging to inspire new designs.

ST review designed membrane channel **pore**

IT Membranes (biological)

Pore
(designed membrane channels and **pores**)

IT Ion channel
RL: ANT (Analyte); ANST (Analytical study)
(designed membrane channels and **pores**)

RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Akerfeldt, K; Acc Chem Res 1993, V26, P191 HCAPLUS
- (2) Al-yahyaee, S; Bioconjugate Chem 1996, V7, P451 HCAPLUS
- (3) Andersen, O; J Am Chem Soc 1998, V120, P5142 HCAPLUS
- (4) Bayley, H; Current Biol 1997, V7, PR763 HCAPLUS
- (5) Bayley, H; Sci Am 1997, V277, P62 HCAPLUS
- (6) Bhakdi, S; Med Microbiol Immunol 1993, V182, P167 HCAPLUS
- (7) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (8) Buchanan, S; Nat Struct Biol 1999, V6, P56 HCAPLUS
- (9) Cane, D; Science 1998, V282, P63 HCAPLUS
- (10) Chang, C; Chem Biol 1995, V2, P391 HCAPLUS
- (11) Chang, G; Science 1998, V282, P2220 HCAPLUS
- (12) Cheley, S; Protein Eng 1997, V10, P1433 HCAPLUS
- (13) Clark, T; J Am Chem Soc 1995, V117, P12364 HCAPLUS
- (14) Clark, T; J Am Chem Soc 1998, V120, P651 HCAPLUS
- (15) Cornell, B; Nature 1997, V387, P580 HCAPLUS
- (16) Dickinson, T; Nature 1996, V382, P687
- (17) Doyle, D; Science 1998, V280, P69 HCAPLUS
- (18) England, P; Proc Natl Acad Sci USA 1997, V94, P11025 HCAPLUS
- (19) Ferguson, A; Science 1998, V282, P2215 HCAPLUS
- (20) Fernandez, T; Nat Biotechnol 1998, V16, P418 HCAPLUS
- (21) Futaki, S; Tetrahedron Lett 1997, V38, P7071 HCAPLUS
- (22) Gallivan, J; Chem Biol 1997, V4, P739 HCAPLUS
- (23) Granja, J; J Am Chem Soc 1994, V116, P10785 HCAPLUS
- (24) Griffin, B; Science 1998, V281, P269 HCAPLUS
- (25) Gritsch, S; Langmuir 1998, V14, P3118 HCAPLUS
- (26) Hartgerink, J; Chem Eur J 1998, V4, P1367 HCAPLUS
- (27) Jaikaran, D; J Phys Chem 1995, V99, P13352 HCAPLUS
- (28) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (29) Kasianowicz, J; to be published in Biophys J 1999
- (30) Kim, H; J Am Chem Soc 1998, V120, P4417 HCAPLUS
- (31) Knowles, J; Science 1987, V236, P1252 HCAPLUS
- (32) Koeppe, R; Annu Rev Biophys Biomol Struct 1996, V25, P231 HCAPLUS
- (33) Lear, J; J Am Chem Soc 1997, V119, P3212 HCAPLUS
- (34) Lee, S; Biochemistry 1997, V36, P3782 HCAPLUS
- (35) Lien, L; J Am Chem Soc 1996, V118, P12222 HCAPLUS
- (36) Locher, K; Cell 1998, V95, P771 HCAPLUS
- (37) Lonergan, M; Chem Mat 1996, V8, P2298 HCAPLUS
- (38) Matsubara, A; J Chem Soc Chem Commun 1996, P2069 HCAPLUS
- (39) Meillon, J; Angew Chem Int Ed Engl 1997, V36, P967 HCAPLUS
- (40) Miller, J; Neuron 1998, V20, P619 HCAPLUS
- (41) Mingarro, I; Trends Biotechnol 1997, V15, P432 HCAPLUS

- (42) Montal, M; Annu Rev Biophys Biomol Struct 1995, V24, P31 HCAPLUS
 (43) Montal, M; FEBS Lett 1993, V320, P261 HCAPLUS
 (44) Mootz, H; Curr Opin Chem Biol 1997, V1, P543 HCAPLUS
 (45) Motesharei, K; J Am Chem Soc 1997, V119, P11306 HCAPLUS
 (46) Mutter, M; Cellular Molec Life Sci 1997, V53, P851 HCAPLUS
 (47) Oiki, S; Biophys J 1994, V66, P1823 HCAPLUS
 (48) Olson, R; to be published in Nat Struct Biol 1999
 (49) Otto-Bruc, A; Proc Natl Acad Sci USA 1998, V95, P15014 HCAPLUS
 (50) Palmer, M; EMBO J 1998, V17, P1598 HCAPLUS
 (51) Pan, P; FEBS Lett 1997, V405, P81 HCAPLUS
 (52) Panchal, R; Nat Biotechnol 1996, V14, P852 HCAPLUS
 (53) Pawlak, M; Protein Sci 1994, V3, P1788 HCAPLUS
 (54) Pederzoli, C; Bioconjugate Chem 1995, V6, P166 HCAPLUS
 (55) Raguse, B; Langmuir 1998, V14, P648 HCAPLUS
 (56) Russo, M; Nat Biotechnol 1997, V15, P278 HCAPLUS
 (57) Sackmann, E; Science 1996, V271, P43 HCAPLUS
 (58) Schmid, B; Protein Sci 1998, V7, P1603 HCAPLUS
 (59) Schuster, B; Biochim Biophys Acta 1998, V1370, P280 HCAPLUS
 (60) Schuster, B; Biochim Biophys Acta 1998, V1369, P51 HCAPLUS
 (61) Scrimin, P; J Am Chem Soc 1996, V118, P2505 HCAPLUS
 (62) Sleytr, U; Trends Biotechnol 1997, V15, P20 HCAPLUS
 (63) Song, L; Science 1996, V274, P1859 HCAPLUS
 (64) Tuchscherer, G; Biopolymers 1998, V47, P63 HCAPLUS
 (65) Valeva, A; EMBO J 1996, V15, P1857 HCAPLUS
 (66) Voyer, N; J Chem Soc Perkin Trans 2 1997, P1469 HCAPLUS
 (67) Walker, B; Chem Biol 1995, V2, P99 HCAPLUS
 (68) Walt, D; Acc Chem Res 1998, V31, P267 HCAPLUS
 (69) Willner, I; Angew Chem Int Ed Engl 1996, V35, P367 HCAPLUS
 (70) Woolley, G; Biophys J 1997, V73, P2465 HCAPLUS
 (71) Woolley, G; Biophys J 1997, V73, P770 HCAPLUS
 (72) You, S; Biochemistry 1996, V35, P6225 HCAPLUS

L82 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:96264 HCAPLUS

DN 130:165159

TI Designed **staphylococcal hemolysin protein pores** as components for metal **biosensors**

IN **Bayley, Hagan**; Braha, Orit; Kasianowicz, John; Gouaux, Eric

PA University of Massachusetts, USA

SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-195

ICS C07K014-305; C07K014-31; G01N033-20; G01N033-48

CC 9-7 (Biochemical Methods)

Section cross-reference(s): 6, 50, 72, 79

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9905167	A1	19990204	WO 1998-US15354	19980724
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9885862	A1	19990216	AU 1998-85862	19980724
PRAI	US 1997-53737P	P	19970725		
	WO 1998-US15354	W	19980724		

AB This invention features a mutant **staphylococcal alpha hemolysin (.alpha.HL) polypeptide** contg. a heterologous metal-binding amino acid. The **polypeptide** assembles into a heteroheptameric **pore** assembly in the presence of a wild type **.alpha.HL polypeptide**. Preferably, the metal-binding amino acid occupies a position in a transmembrane channel of the heteroheptameric **pore** assembly, e.g., an amino acid in the stem domain of WT **.alpha.HL** is substituted with a heterologous metal-binding amino acid. More preferably, the metal-binding amino acid

- projects into the lumen of the transmembrane channel.
- ST **hemolysin staphylococcal peptide mutant**
channel pore metal biosensor
- IT **Biosensors**
Electrodes
Explosives
Mutation
Pore
Pore structure
Protein sequences
Quaternary structure (protein)
Self-association
Staphylococcus
(designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT Metals, analysis
Organic compounds, analysis
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT Amino acids, analysis
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT Ion channel
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); DEV (Device component use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT **.alpha.-Hemolysins**
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); DEV (Device component use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT Diffusion
(pore; designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT 220376-63-6 220376-64-7 220376-65-8
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); DEV (Device component use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT 7440-02-0, Nickel, analysis 7440-43-9, Cadmium, analysis 7440-48-4, Cobalt, analysis 7440-50-8, Copper, analysis 7440-66-6, Zinc, analysis 14701-22-5, Nickel(2+), analysis 15158-11-9, Copper(2+), analysis 22537-48-0, Cadmium(2+), analysis 22541-53-3, Cobalt(2+), analysis 23713-49-7, Zinc(2+), analysis
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(designed **staphylococcal hemolysin protein pores** as components for metal biosensors)
- IT 52-90-4, L-Cysteine, analysis 56-45-1, L-Serine, analysis 56-84-8, L-Aspartic acid, analysis 56-86-0, L-Glutamic acid, analysis 60-18-4, L-Tyrosine, analysis 63-68-3, L-Methionine, analysis 71-00-1, L-Histidine, analysis 72-19-5, L-Threonine, analysis 73-22-3, L-Tryptophan, analysis

RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); DEV (Device component use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(designed **staphylococcal hemolysin protein pores** as components for metal **biosensors**)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bayley; US 5777078 A 1998 HCAPLUS

L82 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:74251 HCAPLUS

DN 130:248484

TI Genetically engineered metal ion binding sites on the outside of a channel's transmembrane .beta.-barrel

AU Kasianowicz, John J.; Burden, Daniel L.; Han, Linda C.; Cheley, Stephen; Bayley, Hagan

CS Biotechnology Division, National Institute of Standards and Technology, Gaithersburg, MD, 20899, USA

SO Biophys. J. (1999), 76(2), 837-845

CODEN: BIOJAU; ISSN: 0006-3495

PB Biophysical Society

DT Journal

LA English

CC 6-3 (General Biochemistry)

AB We are exploring the ability of genetically engineered versions of the **Staphylococcus aureus .alpha.-hemolysin (.alpha.HL)** ion channel to serve as rationally designed **sensor** components for analytes including divalent cations. We show here that neither the hemolytic activity nor the single channel current of wild-type **.alpha.HL** was affected by [Zn(II)] .ltoreq.1 mM. Binding sites for the divalent cations were formed by altering the no. and location of coordinating side chains, e.g., histidines and aspartic acids, between positions 126 and 134, inclusive. Several mutant **.alpha.HLs** exhibited Zn(II)-induced current noise that varied with Zn(II) concn. At a fixed divalent cation concn., the current fluctuation kinetics depended on the analyte type, e.g., Zn(II), Cu(II), Ni(II), and Co(II). We also show that the ability of Zn(II) to change the mutant channel current suggests that the **pore's** topol. is .beta.-sheet and that position 130 is near the turn at the trans mouth. Both conclusions are consistent with the crystal structure of WT-**.alpha.HL oligomerized** in detergent. Our results, in the context of the channel's crystal structure, suggest that conductance blockades were caused by Zn(II) binding to the outside surface of the **pore**. Thus, analyte-induced current blockades alone might not establish whether an analyte binding site is inside a **pore**.

ST **hemolysin** ion channel engineered divalent cation **sensor**

IT Electric conductivity (biological)

Protein engineering

.beta.-Barrel

(genetically engineered metal ion binding sites on outside of a channel's transmembrane .beta.-barrel)

IT **.alpha.-Hemolysins**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(genetically engineered metal ion binding sites on outside of a channel's transmembrane .beta.-barrel)

IT 7440-02-0, Nickel, biological studies 7440-48-4, Cobalt, biological studies 7440-50-8, Copper, biological studies 7440-66-6, Zinc, biological studies

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(genetically engineered metal ion binding sites on outside of a channel's transmembrane .beta.-barrel)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Akabas, M; Biochemistry 1992, V34, P12496

(2) Akabas, M; Science 1992, V258, P307 HCAPLUS

(3) Altenbach, C; Science 1990, V248, P1088 HCAPLUS

- (4) Arnold, F; Science 1991, V252, P1796 HCAPLUS
- (5) Backx, P; Science 1992, V257, P248 HCAPLUS
- (6) Barranger-Mathys, M; Biochemistry 1996, V35, P498 HCAPLUS
- (7) Bezrukov, S; Eur Biophys J 1997, V6, P471
- (8) Bezrukov, S; Macromolecules 1996, V29, P8517 HCAPLUS
- (9) Bezrukov, S; Phys Rev Lett 1993, V70, P2352 HCAPLUS
- (10) Braha, O; Chem Biol 1997, V4, P497 HCAPLUS
- (11) Cheley, S; Protein Eng 1997, V10, P1433 HCAPLUS
- (12) Chen, X; J Gen Physiol 1996, V108, P363 HCAPLUS
- (13) Cornell, B; Nature (Lond) 1997, V387, P580 HCAPLUS
- (14) DeFelice, L; An Introduction to Membrane Noise 1981
- (15) Fairweather, N; Infect Immun 1983, V41, P1112 HCAPLUS
- (16) Gegenheimer, P; Methods in Enzymology 1990, V182, P193
- (17) Gouaux, J; Proc Natl Acad Sci USA 1994, V91, P12828 HCAPLUS
- (18) Gray, G; Infect Immun 1984, V46, P615 HCAPLUS
- (19) Hille, B; Ionic Channels of Excitable Membranes 2nd ed 1992
- (20) Kasianowicz, J; Biophys J 1995, V69, P94 HCAPLUS
- (21) Kasianowicz, J; MRS Symp 1994, V330, P217 HCAPLUS
- (22) Kasianowicz, J; Proc Natl Acad Sci USA 1996, V93, P13770 HCAPLUS
- (23) Korchew, Y; J Membr Biol 1995, V147, P233 HCAPLUS
- (24) Krasilnikov, O; FEMS Microbiol Immunol 1992, V105, P93
- (25) Krasilnikov, O; J Membr Biol 1997, V156, P157 HCAPLUS
- (26) Kunkel, T; Proc Natl Acad Sci USA 1985, V82, P488 HCAPLUS
- (27) Menestrina, G; J Membr Biol 1986, V90, P177 HCAPLUS
- (28) Montal, M; Proc Natl Acad Sci USA 1972, V65, P3561
- (29) Palmer, M; J Biol Chem 1993, V268, P11959 HCAPLUS
- (30) Parsegian, V; Nature (Lond) 1969, V221, P844
- (31) Pietrobon, D; Nature (Lond) 1988, V333, P373 HCAPLUS
- (32) Prod'homme, B; Nature (Lond) 1987, V329, P243 MEDLINE
- (33) Ramirez-Latorre, J; Nature (Lond) 1996, V380, P347 HCAPLUS
- (34) Root, M; Science 1994, V265, P1852 HCAPLUS
- (35) Song, L; Science 1996, V274, P1859 HCAPLUS
- (36) Stevens, C; Nature (Lond) 1977, V270, P391 MEDLINE
- (37) Todd, A; Proteins 1989, V6, P294 HCAPLUS
- (38) Valeva, A; EMBO J 1996, V15, P1857 HCAPLUS
- (39) Valeva, A; Proc Natl Acad Sci USA 1997, V94, P11607 HCAPLUS
- (40) Walker, B; J Biol Chem 1992, V267, P10902 HCAPLUS
- (41) Walker, B; Protein Eng 1994, V7, P655 HCAPLUS

L82 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:545947 HCAPLUS

DN 127:217192

TI Designed **protein pores** as components for
biosensors

AU Braha, Orit; Walker, Barbara; Cheley, Stephen; Kasianowicz, John J.; Song,
Langzhou; Gouaux, J. Eric; **Bayley, Hagan**

CS Department of Medical Biochemistry and Genetics, Texas AandM Health
Science Center, College Station, TX, 77843-1114, USA

SO Chem. Biol. (1997), 4(7), 497-505

CODEN: CBOLE2; ISSN: 1074-5521

PB Current Biology

DT Journal

LA English

CC 9-1 (Biochemical Methods)

AB There is a pressing need for new **sensors** that can detect a variety of analytes, ranging from simple ions to complex compds. and even microorganisms. The devices should offer sensitivity, speed, reversibility and selectivity. Given these criteria, **protein pores**, remodeled so that their transmembrane conductances are modulated by the assocn. of specific analytes, are excellent prospects as components of **biosensors**. Structure-based design and a sepn. method that employs targeted chem. modification have been used to obtain a heteromeric form of the bacterial **pore-forming protein staphylococcal .alpha.-hemolysin**, in which one of the seven subunits contains a binding site for a divalent metal ion, M(II), which serves as a prototypic analyte. The single-channel current

of the heteromer in planar bilayers is modulated by nanomolar Zn(II). Other M(II)s modulate the current and produce characteristic signatures. In addn., heteromers contg. more than one mutant subunit exhibit distinct responses to M(II)s. Hence, a large collection of responsive **pores** can be generated through subunit diversity and combinatorial assembly. Engineered **pores** have several advantages as potential **sensor** elements: sensitivity is in the nanomolar range; analyte binding is rapid (diffusion limited in some cases) and reversible; strictly selective binding is not required because single-channel recordings are rich in information; and for a particular analyte, the dissocn. rate const., the extent of channel block and the voltage-dependence of these parameters are distinguishing, while the frequency of partial channel block reflects the analyte concn. A single **sensor** element might, therefore, be used to quantitate more than one analyte at once. The approach described here can be generalized for addnl. analytes.

ST **protein pore biosensor**

IT **Biosensors**

(designed **protein pores** as components for **biosensors**)

IT **Proteins** (general), uses

.alpha.-Hemolysins

RL: DEV (Device component use); USES (Uses)

(designed **protein pores** as components for **biosensors**)

L82 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:304450 HCAPLUS

DN 124:335771

TI **Pore-forming proteins** with built-in triggers and switches

AU **Bayley, Hagan**

CS Worcester Foundation for Biomedical Research, Shrewsbury, MA, 01545, USA

SO Proc. SPIE-Int. Soc. Opt. Eng. (1996), 2716(Smart Materials Technologies and Biomimetics), 313-316

CODEN: PSISDG; ISSN: 0277-786X

DT Journal; General Review

LA English

CC 6-0 (General Biochemistry)

Section cross-reference(s): 3

AB A review, with 9 refs. Genetic engineering and targeted chem. modification are being used to produce **polypeptides** with **pore-forming** activity that can be triggered or switched on-and-off by biochem., chem. or phys. stimuli. The principal target of our studies has been the **.alpha.-hemolysin** (**.alpha.HL**) from the bacterium **Staphylococcus aureus**. The remodeled **hemolysins** include protease-activated **pores**, metal-regulated **pores**, **pores** that are activated by chem. alkylation and **pores** that are turned on with light. These **polypeptides** have several potential applications. For example, they might serve as components of **sensors** or they might be useful for mediating the controlled release of encapsulated drugs.

ST **protein pore forming hemolysin alpha**
review

IT **Proteins**, specific or class

RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation)

(**pore-forming**, **pore-forming proteins** with built-in triggers and switches)

IT **Hemolysins**

RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation)

(**.alpha.-**, **pore-forming proteins** with built-in triggers and switches)

L82 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:48968 HCAPLUS

DN 124:109804

- TI **Pore-forming proteins** with built-in triggers and switches
- AU **Bayley, Hagan**
- CS Worcester Foundation Biomedical Research, Shrewsbury, MA, 01545, USA
- SO Bioorg. Chem. (1995), 23(4), 340-54
CODEN: BOCMBM; ISSN: 0045-2068
- DT Journal; General Review
- LA English
- CC 6-0 (General Biochemistry)
- AB A review, with 72 refs. The self-assembling, **pore-forming protein .alpha.-hemolysin** is a monomeric, 293-amino-acid, water-sol. **polypeptide** that forms heptameric **pores** of 1- to 2-nm internal diam. in lipid bilayers. By genetic engineering and targeted chem. modification, the authors have produced **.alpha.-hemolysin** in which **pore-forming** activity can be triggered or switched on and off by biochem., chem., or phys. stimuli. These remodeled mols. include protease-activated **pores**, metal-regulated **pores**, **pores** that are activated by chem. alkylation, and **pores** that are turned on with light. Engineered **.alpha.-hemolysins** have potential applications that include acting as components of **sensors** for various analytes, mediating the controlled release of drugs and forming building blocks for agents that selectivity damage malignant cells.
- ST **hemolysin alpha pore** review
- IT **Hemolysins**
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(.alpha.-, **pore-forming proteins** with built-in triggers and switches)
- L82 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2002 ACS
- AN 1995:77803 HCAPLUS
- DN 122:182287
- TI Genetically engineered **pores** as metal **biosensors**
- AU Kasianowicz, John; Walker, Barbara; Krishnasastri, Musti; **Bayley, Hagan**
- CS Biotechnology Division, NIST, Gaithersburg, MD, 20899, USA
- SO Mater. Res. Soc. Symp. Proc. (1994), 330(Biomolecular Materials by Design), 217-23
CODEN: MRSPDH; ISSN: 0272-9172
- DT Journal
- LA English
- CC 9-2 (Biochemical Methods)
Section cross-reference(s): 3
- AB The authors are adapting **proteins** that form **pores** in lipid bilayers for use as components of **biosensors**. Specifically, the authors have produced genetically engineered variants of the **.alpha.-hemolysin (.alpha.HL)** from **Staphylococcus aureus** with properties that are sensitive to low concns. of divalent cations. For example, the **pore-forming** activity of one mutant (**.alpha.HL-H5**: residues 130-134 inclusive replaced with histidine) is inhibited by Zn²⁺ at concns. as low as 1 .mu.M, as judged by the redn. in its ability to lyse rabbit red blood cells and to increase the conductance of planar lipid bilayer membranes. When **.alpha.HL-H5** is added to the aq. phase bathing one side of a planar membrane, the subsequent addn. of 100 .mu.M Zn²⁺ to either side blocks the **pores** that form. This result suggests that at least part of the mutated region lines the channel lumen. Ca²⁺ and Mg²⁺ do not block the channel and therefore the H5 mutation confers a degree of analyte specificity to the **.alpha.HL pore**. The results suggest that genetically engineered **pores** have great promise for the rapid and sensitive detection of metal cations and the authors discuss the merits and potential limitations for their use in this application. Specifically, the authors examine the issues of selectivity, sensitivity, response time, dynamic range and longevity. Some of these properties are interdependent. For example, the goals of high sensitivity

- and rapid response time can be in conflict.
- ST genetically engineered **pore** metal cation **biosensor**;
hemolysin pore forming metal cation **biosensor**
- IT **Biosensors**
(cation sensitive; genetically engineered **pores** as metal **biosensors**)
- IT Genetic engineering
(genetically engineered **pores** as metal **biosensors**)
- IT **Staphylococcus aureus**
(**hemolysin** from; genetically engineered **pores** as metal **biosensors**)
- IT Membrane, biological
(bilayer, lipid, **pores** formed in; genetically engineered **pores** as metal **biosensors**)
- IT Cations
(divalent, genetically engineered **pores** as metal **biosensors**)
- IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**pore**-forming, genetically engineered **pores** as metal **biosensors**)
- IT **Hemolysins**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(.**alpha.**-, genetically engineered, **pore**-forming; genetically engineered **pores** as metal **biosensors**)
- IT 14127-61-8, Ca²⁺, analysis 22537-22-0, Mg²⁺, analysis 23713-49-7, Zn²⁺, analysis
RL: ANT (Analyte); ANST (Analytical study)
(genetically engineered **pores** as metal **biosensors**)
- L82 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:529301 HCAPLUS
DN 121:129301
TI A **pore**-forming **protein** with a metal-actuated switch
AU Walker, Barbara; Kasianowicz, John; Krishnasastri, Musti; Bayley, Hagan
CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
SO Protein Eng. (1994), 7(5), 655-62
CODEN: PRENE9; ISSN: 0269-2139
DT Journal
LA English
CC 9-16 (Biochemical Methods)
AB **Staphylococcal .alpha.-hemolysin**, a **pore**-forming exotoxin, is a **polypeptide** of 293 amino acids that is secreted by **Staphylococcus aureus** as a water-sol. monomer. It assembles to form hexameric **pores** in lipid bilayers. Previous studies of **pore** formation have established the involvement of a central glycine-rich loop. Here, the authors show that when five consecutive histidine residues replace amino acids 130-134 at the midpoint of the loop, they provide a switch with which **pore** activity can be (i) turned off by micromolar concns. of divalent zinc ions and (ii) turned back on with the chelating agent EDTA. Planar bilayer recordings show that Zn²⁺ and EDTA can act on open channels from either side of the bilayer and thus demonstrate that the central loop lines part of the conductive pathway. The authors' results suggest that genetically-engineered **pore**-forming **proteins** might make useful components of metal ion **sensors**
- ST **staphylococcal hemolysin** metal actuated switch; zinc **protein** histidine metal switch; **pore** forming **protein** metal switch
- IT **Proteins**, specific or class
RL: ANST (Analytical study)
(**pore**-forming, metal-actuated switch in)

- IT **Staphylococcus aureus**
(.alpha.-hemolysin from, pore
activity-controlling metal-actuated switch for)
- IT **Hemolysins**
RL: ANST (Analytical study)
(.alpha.-, staphylococcal, pore
activity-controlling metal-actuated switch in)
- IT 71-00-1, Histidine, biological studies
RL: BIOL (Biological study)
(amino acids in staphylococcal .alpha.-
hemolysin replaced by, metal-actuated switch in relation to)
- IT 7440-66-6, Zinc, biological studies
RL: BIOL (Biological study)
(pore activity-controlling switch response to, in
staphylococcal .alpha.-hemolysin)
- L82 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:426821 HCAPLUS
DN 119:26821
TI Monolayers from genetically engineered **protein pores**
AU **Bayley, Hagan**
CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
SO Mater. Res. Soc. Symp. Proc. (1991), 218 (Materials Synthesis Based on
Biological Processes), 69-74
CODEN: MRSPDH; ISSN: 0272-9172
DT Journal
LA English
CC 16-9 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3, 6
AB A selection of microscopic **pores** is being made by genetic
manipulation of a bacterial channel **protein, .alpha.-
hemolysin (.alpha.-HL)**. It will include: **pores**
with different internal diams., with differential selectivity for the
passage of classes of mols., and with different gating properties. The
pores will be made into monolayers and incorporated into materials
such as thin films to confer novel permeability properties upon them.
Such products will have several technol. applications, for example as mol.
filters in **sensors** or as components of optically gated devices
in electronics.
ST genetic engineering **alpha hemolysin monolayer
pore**
IT Gene, microbial
RL: PROC (Process)
(for .alpha.-hemolysin of **Staphylococcus
aureus**, genetic engineering of, for formation of **pore
-contg. monolayers**)
IT Mutation
(of .alpha.-hemolysin gene of
Staphylococcus aureus, for formation of **pore
-contg. monolayers**)
IT Genetic engineering
(of .alpha.-hemolysin of **Staphylococcus
aureus**, for formation of **pore-contg. monolayers**)
IT **Staphylococcus aureus**
(.alpha.-hemolysin of, genetic engineering of, for
formation of **pore-contg. monolayers**)
IT **Hemolysins**
RL: PROC (Process)
(.alpha.-, genetic engineering of, for formation of
pore-contg. monolayers)
IT Conformation and Conformers
(.alpha.-helical, of .alpha.-hemolysin of
Staphylococcus aureus, pore formation in
relation to)
IT Conformation and Conformers
(.beta.-bend, of .alpha.-hemolysin of

Staphylococcus aureus, pore formation in relation to)
 IT Conformation and Conformers
 (.beta.-sheet, of .alpha.-hemolysin of
Staphylococcus aureus, pore formation in relation to)

=> d his

(FILE 'HOME' ENTERED AT 14:25:36 ON 19 MAR 2002)
 SET COST OFF

FILE 'BIOSIS' ENTERED AT 14:25:46 ON 19 MAR 2002

E BAYLEY H/AU
 L1 139 S E3,E4,E6
 E HOWORKA S/AU
 L2 12 S E3-E5
 E MOVILEANU L/AU
 L3 25 S E3,E4
 L4 160 S L1-L3
 L5 15 S L4 AND ?SENSOR?
 L6 13 S L5 AND ?PORE?
 L7 9 S L5 AND (ALPHA OR ALFA) (L) (HEMOLYSIN? OR HAEMOLYSIN? OR HEAMOL
 L8 9 S L5 AND (HEMOLYSIN? OR HAEMOLYSIN? OR HEAMOLYSIN?)
 L9 9 S L7,L8 AND L6
 L10 6 S L5,L6 NOT L9
 SEL DN AN 5 6
 L11 4 S L10 NOT E1-E4
 L12 13 S L7,L8,L11 AND L1-L11
 L13 8 S L12 AND (?PEPTIDE? OR PROTEIN OR SEQUENC? OR (10054 OR 10064)
 L14 8 S L12 AND STAPHYLOC?
 L15 10 S L13,L14
 L16 3 S L12 NOT L15
 L17 13 S L15,L16 AND (?SENSOR? OR ?SENSING OR ?OLIGO?)
 L18 9 S L15,L16 AND ALPHA?
 L19 13 S L12-L18

FILE 'HCAPLUS' ENTERED AT 14:35:09 ON 19 MAR 2002

E BAYLEY H/AU
 L20 132 S E3,E6-E10
 E HOWORKA S/AU
 L21 13 S E3,E5-E7
 E MOVILEANU L/AU
 L22 29 S E3,E4
 L23 14253 S BIOSENS?
 L24 103970 S SENSOR
 E BIOSENSOR/CT
 E E4+ALL
 L25 52868 S E6+NT
 L26 329 S E12+NT
 L27 206371 S E5+NT
 L28 22 S L20-L22 AND L23-L27
 L29 7543 S PROTEIN(L)PORE
 L30 1855 S (PEPTIDE OR POLYPEPTIDE) (L) PORE
 L31 8402 S L29,L30
 L32 932 S (ALPHA OR ALFA) (L) (HEMOLYSIN? OR HAEMOLYSIN? OR HEAMOLYSIN?)
 E ALPHA-HEMOLYSIN/CT
 E E4+ALL
 L33 355 S E2
 E E2+ALL
 L34 3391 S E3
 E E2+ALL
 L35 4528 S E2+NT
 L36 199 S L31 AND L32-L35
 L37 52 S L36 AND STAPHYLOC?

L38 26 S L37 AND (PROTEIN OR ?PEPTIDE) (5A) PORE
 E STAPHYLOCOCCUS/CT
 E E3+ALL
 L39 24392 S E5+NT
 L40 52623 S E5,E7/BI
 L41 41648 S E8-E85/BI
 L42 39 S L36 AND L39-L41
 L43 18 S L42 AND (PROTEIN OR ?PEPTIDE?) (5A) PORE
 L44 27 S L38,L43
 L45 25 S L37,L42 NOT L44
 L46 20 S L28 AND L29-L45
 L47 19 S L28 AND (HEMOLYSIN? OR HAEMOLYSIN? OR HEAMOLYSIN?)
 L48 12 S L28 AND (STAPHYLOC? OR L39-L41)
 L49 17 S L28 AND (PROTEIN? OR ?PEPTIDE?)
 L50 5 S L28 AND ?OLIGO?
 L51 22 S L28,L46-L50

FILE 'HCAPLUS, BIOSIS' ENTERED AT 14:54:38 ON 19 MAR 2002

L52 22 DUP REM L51 L19 (13 DUPLICATES REMOVED)

FILE 'WPIX' ENTERED AT 14:54:49 ON 19 MAR 2002

L53 383390 S SENSOR OR BIOSENSOR OR BIO SENSOR
 L54 37 S L53 AND (PROTEIN? OR ?PEPTIDE?) (L) PORE
 L55 217 S L53 AND (B04-C01? OR C04-C01?)/MC
 L56 12 S L55 AND PORE
 L57 40 S L54,L56
 E BAYLEY H/AU
 L58 5 S E3,E6
 E HOWORKA S/AU
 L59 2 S E3,E4
 E MOVILEANU L/AU
 L60 1 S E3
 L61 2 S L53 AND L58-L60
 L62 4 S L57 AND STAPHYLOC?
 L63 1888 S L53 AND ?LYSIN?
 L64 5 S L63 AND L57
 L65 2 S L64 AND (HEMOLYSIN? OR HEAMOLYSIN? OR HAEMOLYSIN?)
 L66 4 S L61,L62,L65
 L67 2 S L53 AND (HEMOLYSIN? OR HEAMOLYSIN? OR HAEMOLYSIN?)
 L68 4 S L66,L67
 L69 36 S L57 NOT L68
 SEL DN AN 24 25 L69
 L70 2 S L69 AND E1-E5
 L71 6 S L68,L70

FILE 'WPIX' ENTERED AT 15:12:17 ON 19 MAR 2002

FILE 'HCAPLUS' ENTERED AT 15:12:33 ON 19 MAR 2002

L72 267465 S L53 OR L23-L27
 L73 154 S L72 AND (?PEPTIDE? OR PROTEIN?) (L) PORE
 L74 151 S L72 AND L31
 L75 154 S L73,L74
 L76 16 S L75 AND L32-L35
 L77 24 S L51,L76
 L78 201 S L72 AND (?PEPTIDE? OR PROTEIN?) AND PORE
 L79 17 S L32-L35 AND L78
 L80 24 S L77,L79
 L81 23 S L80 AND PORE
 L82 24 S L80-L81

FILE 'HCAPLUS' ENTERED AT 15:16:28 ON 19 MAR 2002